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NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded  
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NEWS 17 May 19 PROUSDDR: One FREE connect hour, per account, in both May and June 2004  
NEWS 18 May 12 EXTEND option available in structure searching  
NEWS 19 May 12 Polymer links for the POLYLINK command completed in REGISTRY  
NEWS 20 May 17 FRFULL now available on STN

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FILE 'BIOSIS' ENTERED AT 16:52:04 ON 25 MAY 2004  
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=> s OX102  
L1 0 OX102

=> s OX 102  
L2 0 OX 102

=> s OX2R or OX2 receptor?  
L3 196 OX2R OR OX2 RECEPTOR?

=> s I3 and antibody?  
L4 10 L3 AND ANTIBOD?

=> dup rem l4  
PROCESSING COMPLETED FOR L4  
L5 7 DUP REM L4 (3 DUPLICATES REMOVED)

=> d bib abs 1-  
YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:300844 CAPLUS  
DN 138:302651

TI Use of bispecific \*\*\*antibodies\*\*\* to regulate immune responses  
IN Bigler, Michael E.; Cherwinski, Holly; Phillips, Joseph H.  
PA Schering Corporation, USA  
SO PCT Int. Appl., 36 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2003030835 A2 20030417 WO 2002-US32711 20021011  
WO 2003030835 A3 20031009  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003077282 A1 20030424 US 2002-270084 20021011  
PRAI US 2001-329182P P 20011012

AB The authors disclose the use of bispecific \*\*\*antibodies\*\*\* for treating diseases relating to the immune system. Specific examples relate to bispecific \*\*\*antibodies\*\*\* which recognize an activating receptor (e.g., Fc.epsilon.RI) and an inhibiting receptor (e.g., Fc.gamma.RIIB).

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2002:849661 CAPLUS  
DN 137:347560

TI Protein and cDNA sequence of human and mouse cytokine \*\*\*ox2\*\*\*  
\*\*\*receptors\*\*\*  
IN Van der Vuurst de Vries, Anne-Renee; Galibert, Laurent J.  
PA Immunex Corporation, USA  
SO PCT Int. Appl., 64 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2002088164 A1 20021107 WO 2002-US13087 20020425  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-286686P P 20010426  
AB The invention relates to protein and cDNA sequence of human and mouse cytokine \*\*\*ox2\*\*\*. Ox2 is a transmembrane protein, designated as human leukocyte antigen CD200. The receptors are also useful in screening for inhibitors or agonists thereof. The invention further relates to prepn. of \*\*\*antibody\*\*\* for \*\*\*ox2\*\*\*  
\*\*\*receptor\*\*\*

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
AN 2001:548413 BIOSIS  
DN PREV200100548413

TI The electrophysiological analysis of orexin-neurons.  
AU Yamanaka, A. [Reprint author]; Tsujino, N. [Reprint author]; Tominaga, M.; Masu, M. [Reprint author]; Yamamoto, M. [Reprint author]; Katsumoto, T. [Reprint author]; Goto, K. [Reprint author]; Sakurai, T. [Reprint author]

CS University of Tsukuba, Tsukuba, Japan  
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 1679.  
print  
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.  
ISSN: 0190-5295.

DT Conference; (Meeting)  
Conference; Abstract (Meeting Abstract)  
LA English

ED Entered STN: 21 Nov 2001

Last Updated on STN: 25 Feb 2002

AB Orexins (hypocretins) are a pair of neuropeptides that are implicated in energy homeostasis and arousal. The actions of orexins are mediated via two G protein-coupled receptors named the orexin-1 (OX1R) and orexin-2 receptor (\*\*\*OX2R\*\*\*). Prepro-orexin mRNA is upregulated upon fasting, suggesting the orexin system play roles in the maintaining the energy homeostasis. It is difficult to investigate the character of orexin neurons using electrophysiological technique, because to identify orexin neurons morphologically from other neurons is impossible. We tagged orexin neurons in transgenic mice, in which orexin neurons specifically express green fluorescent protein (GFP). We have previously reported transgenic studies in which the 3.2-kb fragment of the 5'-upstream region of the human prepro-orexin gene is sufficient to express the lacZ gene in orexin neurons. Immunohistochemical experiments using anti-orexin \*\*\*antibody\*\*\* revealed that 80% of orexin neurons expressed GFP in two-lines of transgenic mice. Orexin neurons were dissociated from lateral hypothalamus and were adhered on slide glass for electrophysiological experiments. Spontaneous action potential was recorded by whole-cell patch clamp technique using current-clamp mode. Leptin inhibits, while ghrelin activates the activity of orexin neurons. Our present study demonstrated that orexin-containing neurons are sensing peripheral metabolic signals and control feeding behavior and vigilance to maintain energy homeostasis.

L5 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2001:513615 BIOSIS

DN PREV200100513615

TI Orexin-A (OX-A) induced delayed onset of paradoxical sleep (PS) in the rat is mediated via orexin-1 receptors (OX1R).

AU Smith, M. I. [Reprint author]; Piper, D. C. [Reprint author]; Duxon, M. S. [Reprint author]; Upton, N. [Reprint author]

CS Neuroscience, GlaxoSmithKline, Harlow, Essex, UK

SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 1090. print.

Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.

ISSN: 0190-5295.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 7 Nov 2001

Last Updated on STN: 23 Feb 2002

AB The novel neuropeptide OX-A modulates the sleep wake cycle such that intracerebroventricular (icv) application to rats increases arousal, reduces slow wave sleep 2 and PS and delays PS onset (Piper et al. 2000 Eur J Neurosci 12:726-30). The contribution of OX1R and \*\*\*OX2R\*\*\* to this OX-A effect is still unknown. Using the selective OX1R antagonist SB-334867-A (Duxon et al. 2001 Psychopharmacol 153:203-9) we investigate the role of OX1R in OX-A delayed PS onset. Male rats prepared for frontal-occipital electroencephalograph, nuchal muscle electromyograph recording and lateral ventricle cannulae received vehicle or OX-A (10µg) icv at the lights off: on interface in combination with vehicle or SB-334867-A (10 or 30mg/kg ip) 30min pre-icv injection. The latency to onset of the first gtoreq10sec epoch of PS was measured. Following vehicle treatment PS latency was 57±11min. OX-A administration significantly (p<0.05) increased this to 120±25min. Pre-treatment with SB-334867-A at both 10 and 30mg/kg completely reversed the effects of OX-A (64±22 and 62±17min, respectively, p<0.05). SB-334867-A, 10 and 30mg/kg alone, did not significantly (p>0.05) alter PS latency (44±9 and 63±18 min, respectively). An \*\*\*OX2R\*\*\* component to orexin sleep control is evident from its association with the narcoleptic phenotype of the Doberman pinscher (Lin et al. 1999 Cell 98:365-6). The present study with the selective OX1R antagonist SB-334867-A, together with the data of Bourgin et al. 2000 (J Neurosci 20(2):7760-5) showing that an OX1R neutralising \*\*\*antibody\*\*\* reverses OX-A effects on sleep stage architecture, demonstrates that the OX1R also has a role in orexinergic sleep modulation.

L5 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 1

AN 2001:187889 BIOSIS

DN PREV200100187889

TI The unusual distribution of the neuronal/lymphoid cell surface CD200 (OX2) glycoprotein is conserved in humans.

AU Wright, G. J.; Jones, M.; Puklavec, M. J.; Brown, M. H.; Barclay, A. N. [Reprint author]

CS Sir William Dunn School of Pathology, South Parks Road, Oxford, OX1 3RE, UK

SO Immunology, (February, 2001) Vol. 102, No. 2, pp. 173-179. print.

CODEN: IMMUA. ISSN: 0019-2805.

DT Article

LA English

ED Entered STN: 20 Apr 2001

Last Updated on STN: 18 Feb 2002

AB OX2 (CD200) is a type-1 membrane glycoprotein that contains two immunoglobulin superfamily domains and which is expressed on a variety of lymphoid and non-lymphoid cells in the rat. The recent characterization of a receptor for OX2 (\*\*\*OX2R\*\*\* ) on myeloid cells, and the phenotype of an OX2-deficient mouse, suggests that OX2 may regulate myeloid cell activity in anatomically diverse locations. Here we report the tissue

distribution of the human homologue of the rat OX2 glycoprotein using a new monoclonal \*\*\*antibody\*\*\* (mAb), OX104, raised against recombinant human OX2. Human OX2 was expressed at the cell surface of thymocytes, B cells, T cells, neurons, kidney glomeruli, tonsil follicles, the syncytiotrophoblast and endothelial cells. This broad, but not ubiquitous, distribution pattern is very similar to that observed in rats, suggesting that OX2 may regulate myeloid cell activity in a variety of tissues in humans.

L5 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 2

AN 2001:79096 BIOSIS

DN PREV200100079096

TI Distribution of OX2 antigen and \*\*\*OX2\*\*\* \*\*\*receptor\*\*\* within retina.

AU Dick, Andrew D. [Reprint author]; Broderick, Cathryn; Forrester, John V.; Wright, Gavin J.

CS Division of Ophthalmology, Bristol Eye Hospital, University of Bristol, Lower Maudlin Street, Bristol, BS1 2LX, UK

a.dick@bristol.ac.uk

SO IOVS, (January, 2001) Vol. 42, No. 1, pp. 170-176. print

DT Article

LA English

ED Entered STN: 7 Feb 2001

Last Updated on STN: 12 Feb 2002

AB Purpose. OX2 is a member of the immunoglobulin superfamily expressed on a

broad range of tissues including neurons of the central and peripheral nervous systems, thymocytes, and endothelium. The recently identified \*\*\*OX2\*\*\* \*\*\*receptor\*\*\* (\*\*\*OX2R\*\*\* ) is restricted to the surfaces of myeloid lineage cells, including microglia. Functional data have implicated the OX2- \*\*\*OX2R\*\*\* interaction as a myeloid downregulatory signal. The purpose of this study was to determine the distribution and extent of expression of OX2 and its receptor within the retina, a tissue developed to restrain immune-mediated inflammatory damage. Methods. OX2 and \*\*\*OX2R\*\*\* monoclonal \*\*\*antibodies\*\*\* (mAbs) were used to determine OX2 and \*\*\*OX2R\*\*\* protein expression, respectively, by flow cytometry of isolated myeloid-derived cells from normal and inflamed rat retina and by immunohistochemistry of serial sections of rat retina. For comparison, distribution of OX2 was documented using species-specific monoclonal \*\*\*antibodies\*\*\* in mouse and human retina. No \*\*\*OX2R\*\*\* mAbs are available for mouse or human detection. Results. OX2 was expressed on retinal vascular endothelium and glial fibrillary acidic protein (GFAP)-negative neurons in retina and optic nerve and on a subpopulation of CD45+ perivascular and juxta-vascular cells. Within normal retina, \*\*\*OX2R\*\*\* was not detected on myeloid-derived cells. During experimental autoimmune uveoretinitis (EAU), expression of both OX2 and \*\*\*OX2R\*\*\* was noted on infiltrating leukocytes. Conclusions. Taking these results of the distribution of OX2 in normal and \*\*\*OX2R\*\*\* in inflamed retina with other functional data of OX2- \*\*\*OX2R\*\*\* interaction, it is suggested that the OX2- \*\*\*OX2R\*\*\* interaction has the potential to contribute to a novel pathway that suppresses and limits immunologic inflammatory damage within the retina.

L5 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:824408 CAPLUS

DN 133:360278

TI Animal \*\*\*OX2\*\*\* \*\*\*receptor\*\*\* homologs and cDNAs and their uses in diagnosis and therapy

IN Barclay, A. Neil; Brown, Marion H.; Gorman, Daniel M.; Lanier, Lewis L.; Wright, Gavin J.; Chervinski, Holly; Phillips, Joseph H.; Hoek, Robert M.; Sedgwick, Jonathan D.

SA Medical Research Council, UK; Schering Corporation

PO PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2000070045	A1	20001123	WO 2000-US12998	20000511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1177295	A1	20020208	EP 2000-83237	20000511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002543838	T2	20021224	JP 2000-618451	20000511
NZ 515382	A	20040326	NZ 2000-515382	20000511
ZA 2001009315	A	20030212	ZA 2001-9315	20011112
PRAIGB 1999-11123	A	19990513		
GB 1999-25989	A	19991103		
WO 2000-US12998	W	20000511		

AB Nucleic acids encoding mammalian, e.g., primate, receptors of OX2, purified proteins and fragments thereof. \*\*\*Antibodies\*\*\*, both polyclonal and monoclonal, are also provided. Method of using the compns.

for both diagnostic and therapeutic utilities are described.  
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L6 4401 BARCLAY?/AU

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L1 0 S OX102  
L2 0 S OX 102  
L3 196 S OX2R OR OX2 RECEPTOR?  
L4 10 S L3 AND ANTIBOD?  
L5 7 DUP REM L4 (3 DUPLICATES REMOVED)  
L6 4401 S BARCLAY?/AU

=> s l3 and l6  
L7 12 L3 AND L6

=> dup rem l7  
PROCESSING COMPLETED FOR L7  
L8 8 DUP REM L7 (4 DUPLICATES REMOVED)

=> d bib abs 1-  
YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y(N):y

L8 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN  
DUPLICATE 1  
AN 2001:187889 BIOSIS  
DN PREV200100187889  
TI The unusual distribution of the neuronal/lymphoid cell surface CD200 (OX2)  
glycoprotein is conserved in humans.  
AU Wright, G. J.; Jones, M.; Puklavec, M. J.; Brown, M. H.; \*\*\*Barclay, A.\*\*\*  
\*\*\* N.\*\*\* [Reprint author]  
CS Sir William Dunn School of Pathology, South Parks Road, Oxford, OX1 3RE,  
UK  
SO Immunology, (February, 2001) Vol. 102, No. 2, pp. 173-179. print.  
CODEN: IMMUAJ. ISSN: 0019-2805.  
DT Article  
LA English  
ED Entered STN: 20 Apr 2001  
Last Updated on STN: 18 Feb 2002  
AB OX2 (CD200) is a type-1 membrane glycoprotein that contains two  
immunoglobulin superfamily domains and which is expressed on a variety of  
lymphoid and non-lymphoid cells in the rat. The recent characterization  
of a receptor for OX2 (\*\*\*OX2R\*\*\*) on myeloid cells, and the phenotype  
of an OX2-deficient mouse, suggests that OX2 may regulate myeloid cell  
activity in anatomically diverse locations. Here we report the tissue  
distribution of the human homologue of the rat OX2 glycoprotein using a  
new monoclonal antibody (mAb), OX104, raised against recombinant human  
OX2. Human OX2 was expressed at the cell surface of thymocytes, B cells,  
T cells, neurons, kidney glomeruli, tonsil follicles, the  
syncytiotrophoblast and endothelial cells. This broad, but not  
ubiquitous, distribution pattern is very similar to that observed in rats,  
suggesting that OX2 may regulate myeloid cell activity in a variety of  
tissues in humans.

L8 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2000:824408 CAPLUS  
DN 133:360278  
TI Animal \*\*\*OX2\*\*\* \*\*receptor\*\*\* homologs and cDNAs and their uses  
in diagnosis and therapy  
IN \*\*\*Barclay, A. Neil\*\*\*; Brown, Marion H.; Gorman, Daniel M.; Lanier,  
Lewis L.; Wright, Gavin J.; Chervinski, Holly; Phillips, Joseph H.; Hoek,  
Robert M.; Sedgwick, Jonathan D.  
PA Medical Research Council, UK; Schering Corporation  
SO PCT Int. Appl., 142 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2000070045 A1 20001123 WO 2000-US12998 20000511  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,  
CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN,  
IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN,  
MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
EP 1177295 A1 20020206 EP 2000-932337 20000511  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO  
JP 2002543838 T2 20021224 JP 2000-618451 20000511  
NZ 515382 A 20040328 NZ 2000-515382 20000511  
ZA 2001009315 A 20030212 ZA 2001-9315 20011112  
PRAI GB 1999-11123 A 19990513  
GB 1999-25989 A 19991103  
WO 2000-US12998 W 20000511  
AB Nucleic acids encoding mammalian, e.g., primate, receptors of OX2,  
purified proteins and fragments thereof. Antibodies, both polyclonal and  
monoclonal, are also provided. Method of using the compns. for both  
diagnostic and therapeutic utilities are described.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2000:887284 CAPLUS  
DN 134:84009  
TI Down-regulation of the macrophage lineage through interaction with OX2  
(CD200)  
AU Hoek, Robert M.; Ruuls, Sigrid R.; Murphy, Craig A.; Wright, Gavin J.;  
Goddard, Ruth; Zurawski, Sandra M.; Blom, Bianca; Homola, Margit E.;  
Streit, Wolfgang J.; Brown, Marion H.; \*\*\*Barclay, A. Neil\*\*\*;  
Sedgwick, Jonathan D.  
CS DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA,  
94304, USA  
SO Science (Washington, D. C.) (2000), 290(5497), 1768-1771  
CODEN: SCIEAS; ISSN: 0036-8075  
PB American Association for the Advancement of Science  
DT Journal  
LA English  
AB OX2 (CD200) is a broadly expressed membrane glycoprotein, shown here to  
be

important for regulation of the macrophage lineage. In mice lacking  
CD200, macrophage lineage cells, including brain microglia, exhibited an  
activated phenotype and were more numerous. Upon facial nerve  
transection, damaged CD200-deficient neurons elicited an accelerated  
microglial response. Lack of CD200 resulted in a more rapid onset of  
exptl. autoimmune encephalomyelitis (EAE). Outside the brain, disruption  
of CD200-CD200 receptor interaction ptpd. susceptibility to  
collagen-induced arthritis (CIA) in mice normally resistant to this  
disease. Thus, in diverse tissues OX2 delivers an inhibitory signal for  
the macrophage lineage.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS  
RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN  
AN 2001:50733 BIOSIS  
DN PREV200100050733  
TI Macrophage regulation by the B7.1/2 homologue OX2?  
AU Hoek, R. M. [Reprint author]; Ruuls, S. R. [Reprint author]; Homola, M. E.  
[Reprint author]; Brown, M.; Streit, W. J.; Lemckert, F. A.; \*\*\*Barclay,\*\*\*  
\*\*\* A. N.\*\*\*; Sedgwick, J. D. [Reprint author]  
CS DNAX Research Institute, Palo Alto, CA, USA  
SO FASEB Journal, (April 20, 2000) Vol. 14, No. 6, pp. A1232. print.  
Meeting Info.: Joint Annual Meeting of the American Association of  
Immunologists and the Clinical Immunology Society. Seattle, Washington,  
USA. May 12-16, 2000.  
CODEN: FAJOEC. ISSN: 0892-6638.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 24 Jan 2001  
Last Updated on STN: 12 Feb 2002

L8 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN  
DUPLICATE 2  
AN 2000:440556 BIOSIS  
DN PREV20000440556  
TI Lymphoid/neuronal cell surface OX2 glycoprotein recognizes a novel  
receptor on macrophages implicated in the control of their function.  
AU Wright, Gavin J.; Puklavec, Michael J.; Willis, Antony C.; Hoek, Robert  
M.; Sedgwick, Jonathan D.; Brown, Marion H.; \*\*\*Barclay, A. Neil\*\*\*  
[Reprint author]  
CS Sir William Dunn School of Pathology, University of Oxford, South Parks  
Road, Oxford, OX1 3RE, UK  
SO Immunity, (August, 2000) Vol. 13, No. 2, pp. 233-242. print.  
ISSN: 1074-7613.

DT Article  
LA English  
OS Genbank-AF231392; Genbank-AF231393  
ED Entered STN: 18 Oct 2000  
Last Updated on STN: 10 Jan 2002  
AB The OX2 membrane glycoprotein (CD200) is expressed on a broad range of  
tissues including lymphoid cells, neurons, and endothelium. We report the  
characterization of an \*\*\*OX2\*\*\* \*\*receptor\*\*\* (\*\*\*OX2R\*\*\*)  
that is a novel protein restricted to cells of the myeloid lineage. OX2

and its receptor are both cell surface glycoproteins containing two immunoglobulin-like domains and interact with a dissociation constant of 2.5 µM and koff 0.8 s<sup>-1</sup>, typical of many leukocyte protein membrane interactions. Pervanadate treatment of macrophages showed that \*\*\*OX2R\*\*\* could be phosphorylated on tyrosine residues. Blockade of the OX2- \*\*\*OX2R\*\*\* interaction with an \*\*\*OX2R\*\*\* mAb exacerbated the disease model experimental allergic encephalomyelitis. These data, together with data from an OX2-deficient mouse (R. M. Hoek et al., submitted), suggest that myeloid function can be controlled in a tissue-specific manner by the OX2- \*\*\*OX2R\*\*\* interaction.

L8 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
AN 2001:82960 BIOSIS  
DN PREV200100082960  
TI Viral homologues of cell surface proteins OX2 and CD47 have potential to regulate macrophage function.  
AU Wright, G. J. [Reprint author]; Vernon-Wilson, Elizabeth [Reprint author]; Foster, Mildred [Reprint author]; Brown, M. H. [Reprint author]; Barclay, A. N.\*\*\* [Reprint author]  
CS Sir William Dunn School of Pathology, University of Oxford, Oxford, OX1 3RE, UK  
SO Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 50. print. Meeting Info.: Annual Congress of the British Society for Immunology. Harrogate, UK. December 05-08, 2000. British Society for Immunology. CODEN: IMMUA. ISSN: 0019-2805.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 14 Feb 2001  
Last Updated on STN: 12 Feb 2002

L8 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
AN 2001:82882 BIOSIS  
DN PREV200100082882  
TI Interactions of cytoplasmic region of \*\*\*OX2R\*\*\* are consistent with an inhibitory function.  
AU Hutchings, N. J. [Reprint author]; Brooke, G. [Reprint author]; Chalkley, R.; Wright, G. J. [Reprint author]; Brown, M. H. [Reprint author]; Barclay, A. N.\*\*\* [Reprint author]  
CS Sir William Dunn School of Pathology, University of Oxford, Oxford, OX1 3RE, UK  
SO Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 24. print. Meeting Info.: Annual Congress of the British Society for Immunology. Harrogate, UK. December 05-08, 2000. British Society for Immunology. CODEN: IMMUA. ISSN: 0019-2805.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 14 Feb 2001  
Last Updated on STN: 12 Feb 2002

L8 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
AN 2000:513968 BIOSIS  
DN PREV200000513968  
TI The lymphoid/neuronal OX2 glycoprotein interacts with a novel protein expressed by macrophages.  
AU Wright, G. J. [Reprint author]; Brown, M. H. [Reprint author]; Barclay, A. N.\*\*\* [Reprint author]  
CS Sir William Dunn School of Pathology, University of Oxford, Oxford, UK  
SO Tissue Antigens, (2000) Vol. 55, No. Supplement 1, pp. 11. print. Meeting Info.: 7th Workshop and Conference on Human Leucocyte Differentiation Antigens. Harrogate, England, UK. June 20-24, 2000. CODEN: TSANA2. ISSN: 0001-2815.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 29 Nov 2000  
Last Updated on STN: 11 Jan 2002

=> s CD200 (3a) receptor?  
1 FILES SEARCHED...  
L9 35 CD200 (3A) RECEPTOR?

=> s I9 and (antibod? or mAb)  
L10 10 L9 AND (ANTIBOD? OR MAB)

=> dup rem I10  
PROCESSING COMPLETED FOR L10  
L11 6 DUP REM L10 (4 DUPLICATES REMOVED)

=> d bib abs 1-  
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L11 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:757548 CAPLUS  
DN 139:275741  
TI \*\*\*Antibodies\*\*\*, agonists and antagonists to \*\*\*CD200\*\*\*  
\*\*\*receptors\*\*\* for diagnosis and treatment of immune disease, inflammation, infection and cancer

IN Cherwinski, Holly M.; Phillips, Joseph H.; Sedgwick, Jonathon D.; Bigler, Michael E.; Murphy, Craig A.  
PA Schering Corporation, USA  
SO PCT Int. Appl., 58 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003077947	A1	20030925	WO 2003-US7647	20030313
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003223991	A1	20031204	US 2003-389231	20030313
PRAI US 2002-384513P	P	20020315		
AB Abstr. Provided are methods for modulating activity of the immune system using agonists or antagonists of a ***CD200*** ***receptor***. The agonists or antagonists are humanized ***antibodies***, monoclonal ***antibodies***, polyclonal ***antibodies***, ***antibody*** fragments, peptide mimetic of ***antibody***. The ***antibodies***, agonists and antagonists are provided for treatment and diagnosis of immune and autoimmune disorder, inflammation, rheumatoid arthritis, endotoxemia, psoriasis, allergy, infection or cancer.				

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
AN 2003214539 EMBASE  
TI Modulation of \*\*\*CD200\*\*\* \*\*\*receptors\*\*\* as a novel method of immunosuppression.  
SO Expert Opinion on Therapeutic Patents, (1 May 2003) 13/5 (711-715). Refs: 34  
ISSN: 1354-3778 CODEN: EOTPEG  
CY United Kingdom  
DT Journal; Article  
FS 022 Human Genetics  
026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index  
LA English  
SL English  
AB Current methods of therapeutic immunomodulation are unsatisfactory. More effective and safer strategies are needed either to suppress immune responses for the treatment of transplant rejections, autoimmunity and allergy or to boost immunity against infectious diseases and cancer. This patent application proposes a novel approach towards these goals based on targeting \*\*\*CD200\*\*\* \*\*\*receptors\*\*\* (CD200R). Whereas \*\*\*CD200\*\*\* is expressed on lymphoid cells, neurons and endothelium, CD200R are mainly expressed on macrophages and myeloid cells. Crosslinking CD200R with CD200.Fc, an immunoadhesin made up of the CD200 extracellular region fused to the murine IgG2a Fc region or with anti-CD200R monoclonal \*\*\*antibodies\*\*\* (mAbs) can prolong allograft and xenograft survival and ameliorate collagen-induced arthritis in mice. Murine CD200R isoforms were identified by genomic analyses and partially characterised using specific mAbs acting presumably as receptor agonists. Myeloid dendritic cells (DCs) generated in the presence of anti-CD200R isoform mAbs were unable to stimulate the production of IFN- gamma. and cytolytic lymphocytes in a mixed lymphocyte culture but induced the emergence of suppressor cells. When injected prior to transplantation, such DCs were capable of significantly prolonging skin allograft survival. Although the data suggest that CD200R might serve to dampen immune responses, further investigations are required to determine whether this approach would be applicable to human disease situations.

L11 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2002:906505 CAPLUS  
DN 138:12292  
TI Cloning and characterization of mouse \*\*\*CD200\*\*\* \*\*\*receptor\*\*\* variants, and therapeutic use thereof in modulating immune response in animal transplantation and immune diseases  
IN Gorczynski, Reginald M.; Marsden, Philip  
PA Transplantation Technologies Inc., Can.; Trillium Therapeutics Inc.  
SO PCT Int. Appl., 189 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002095030	A2	20021128	WO 2002-CA734	20020524

WO 2002095030 A3 20030821

V: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-292950P P 20010524

US 2002-369862P P 20020405

AB The present invention relates to \*\*\*CD200\*\*\* \*\*receptor\*\*\* isoforms and modulators thereof and their use in methods of immune modulation and pharmaceutical compns. In particular, protein and cDNA sequences for three isoforms of the murine \*\*\*CD200\*\*\* \*\*receptor\*\*\* called CD200R2a, CD200R2b and CD200R3a are provided.

The inventors have also prep. \*\*\*antibodies\*\*\* to the different isoforms of CD200R. Studies of using CD200R \*\*\*antibodies\*\*\*, co-administering the \*\*\*CD200\*\*\* \*\*receptor\*\*\* with a \*\*\*CD200\*\*\* peptide, preferably in the form of a sol. fusion protein, such as CD200Fc, to modulate immune response are presented. The inventors have also shown that administering \*\*\*antibody\*\*\* fragments [e.g. Fab or F(ab')2 fragments] that bind to a \*\*\*CD200\*\*\* \*\*receptor\*\*\* inhibits the immune suppression caused by CD200. Accordingly, in another aspect, the present invention provides a method of inhibiting immune suppression by administering an effective amt. of a \*\*\*CD200\*\*\* \*\*receptor\*\*\* antagonist to a cell or animal in need thereof. Preferably, the antagonist is an agent that inhibits the interaction of the \*\*\*CD200\*\*\* \*\*receptor\*\*\* with \*\*\*CD200\*\*\*.

L11 ANSWER 4 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 2

AN 2002373008 EMBASE

TI Anti-CD200R ameliorates collagen-induced arthritis in mice.

AU Gorczynski R.M.; Chen Z.; Lee L.; Yu K.; Hu J.

CS R.M. Gorczynski, CCRW 2-855, Transplant Research Division, Toronto Hospital, 200 Elizabeth Street, Toronto, Ont. M5G 2C4, Canada

SO Clinical Immunology, (2002) 104/3 (256-264).

Refs: 22

ISSN: 1521-6618 CODEN: CLIIFY

CY United States

DT Journal; Article

FS 026 Immunology, Serology and Transplantation

031 Arthritis and Rheumatism

LA English

SL English

AB Immunization of DBA/1 with 100 .mu.g bovine collagen type II emulsified in Freund's adjuvant, followed by booster injection in incomplete adjuvant at 18 days, leads to development of arthritis in more than 70% of mice by 28 days postinjection. We have previously shown that the novel immunosuppressant molecule CD200Fc (linking an extracellular domain of CD200 with a murine IgG2a Fc region) can suppress induction of disease when given to mice from the time of collagen injection. This occurs in concert with a decrease in the serum levels of anti-collagen IgG (apprx. 50% reduction), with relatively more IgG2b and IgG3, decreased serum levels of TNF-alpha. and IFN-gamma., and decreased production of those same cytokines after re-stimulation of lymphocytes in vitro with collagen. Since CD200 induces suppression following engagement of a receptor (CD200R), known to be expressed on, among other cells, macrophages, we investigated whether infusion of anti-CD200R and/or CD200Fc would ameliorate established disease in DBA mice, when injections were begun following collagen immunization. Our data indicate an arrest of disease following either treatment, with modification of a number of immune parameters (serum and lymphocyte cytokine production) consistent with a general role for CD200: CD200R interactions in the regulation of induction and/or expression of autoimmune disorders. When a higher dose (250 .mu.g/mouse) of anti-CD200R was infused into a group of overtly arthritic mice, a significant (apprx. 50%) decrease in arthritic joint score occurred over the 4-week treatment period. .COPYRG. 2002 Elsevier Science (USA).

L11 ANSWER 5 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 2002239920 EMBASE

TI The same immunoregulatory molecules contribute to successful pregnancy and transplantation.

AU Gorczynski R.M.; Hadidi S.; Yu G.; Clark D.A.

CS Dr. R.M. Gorczynski, CCRW 2-855, Toronto Hospital, 101 College Street W., Toronto, Ont. M5G 2C4, Canada. rgorczynski@uhnres.utoronto.ca

SO American Journal of Reproductive Immunology, (2002) 48/1 (18-26).

Refs: 54

ISSN: 8755-8920 CODEN: AAJID6

CY United Kingdom

DT Journal; Article

FS 010 Obstetrics and Gynecology

028 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LA English

SL English

AB Problem: At least two dendritic cell-associated molecules have been shown to contribute to the successful outcome of organ and tissue allografts in mice, namely CD200 and MD-1. CD200 is up-regulated in rodent transplantation models where successful inhibition of rejection is accomplished, and is believed to signal immunosuppression following engagement of a receptor, CD200R, on macrophages and/or .gamma.-delta. T-cell receptor (.gamma.-delta. TCR(+)) cells MD-1 is implicated in controlling expression of costimulatory molecules including CD80/CD86 which induce an immunorejection response, and thus inhibition of MD-1 expression also facilitates increased graft survival MD-1 also stabilizes expression of CD14, part of the receptor complex for LPS. As well as the inhibition of rejection which follows blockade of MD-1 expression and/or augmentation of CD200 expression, an altered polarization in cytokine production is seen, with increased expression of interleukin-4 (IL-4), IL-10 and transforming growth factor-.beta. (TGF-.beta.), and decreased IL-2, interferon-.gamma. (IFN-.gamma.) and tumor necrosis factor-.alpha. (TNF-.alpha.). Successful pregnancy in allograft mice also depends upon control of graft rejection mechanisms. Proinflammatory T-helper 1 (Th1) cytokines (TNF-.alpha. + IFN-.gamma. + IL-1) have been shown to cause spontaneous abortion in mice by activating a novel prothrombinase, fibrinogen-like peptide (fibrinogen) fg12, which may promote fibrin deposition in the graft rejection process; expression of IL-10, TGF-.beta., and progesterone-induced blocking factor (PIBF) in contrast leads to lowering of abortion rates. Interestingly, the spontaneous abortion rates in abortion-prone CBA x DBA/2 matings and in the low abortion rate CBA x BALB/c matings were lower than the frequency of implantation sites showing fibrin(hi) + fg12 (mRNA)(hi), implying regulation of the pro-abortion consequences of fg12 expression. Methods: We have investigated, by in situ hybridization, CD200, MD-1 and fg12 expression in implantation sites in different strains of mice, and studied the effects of anti-MD-1, anti-CD200 and CD200Fc immunoadhesin on fetal and allograft survival. The role of indoleamine dioxygenase (IDO) was evaluated. Results: CD200 mRNA expression occurred in the same sites as fg12 mRNA. Anti-CD200 \*\*\*antibody\*\*\* raised the abortion rate to predicted levels, and infusion of a CD200 immunoadhesin reduced the abortion rate, as did an anti-MD-1 \*\*\*antibody\*\*\*. The latter also improved organ and tissue graft survival. Suppression by antigen-presenting macrophages triggered by CD200 is dependent upon intact IDO activity. Conclusion: Regulation of CD200 and MD-1 expression may control both pregnancy and allograft survival. .COPYRG. Blackwell Munksgaard, 2002.

L11 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 3

AN 2001:429194 BIOSIS

DN PREV200100429194

TI Transplant tolerance modifying \*\*\*antibody\*\*\* to \*\*\*CD200\*\*\* \*\*receptor\*\*\*, but not \*\*\*CD200\*\*\*, alters cytokine production profile from stimulated macrophages.

AU Gorczynski, Reginald M. [Reprint author]

CS Toronto Hospital, 200 Elizabeth Street, CCRW 2-855, Toronto, ON, M5G2C4, Canada

SO European Journal of Immunology, (August, 2001) Vol. 31, No. 8, pp. 2331-2337. print

CODEN: EJIMAF. ISSN: 0014-2980.

DT Article

LA English

ED Entered STN: 12 Sep 2001

Last Updated on STN: 22 Feb 2002

AB Increased C57BL/6 allograft survival following donor-specific dendritic cell (DC) portal vein (pv) pre-transplant immunization of C3H mice is associated with increased expression of the molecule CD200 on DC, delivery of suppressive signals by CD200+ macrophages, and polarization in cytokine production towards type-2 cytokines. Infusion of anti-mouse CD200 monoclonal \*\*\*antibody\*\*\* abolishes these effects. We have used whole Ig, and F(ab')2 fragments, of anti-CD200 and anti-CD200r \*\*\*mAb\*\*\* to explore the relative signaling role of CD200+ versus CD200r+ cells in suppression of type-1 cytokine production in mixed leukocyte cultures (MLC), and enhanced graft survival in vivo. Simple neutralization of CD200 (even by F(ab')2 \*\*\*antibody\*\*\* ) reversed CD200-mediated suppression. However, only whole anti-CD200r \*\*\*antibody\*\*\* was effective in stimulating suppression from CD200r+ cells. Suppression of cytokine induction following cross-linking of CD200r+ cells in vitro was attenuated by anti-IL-6 \*\*\*mAb\*\*\*. Our data are consistent with the hypothesis that CD200r itself delivers the crucial intracellular signal leading to immunosuppression, a feature likely of importance in autoimmunity and transplantation.

=> d his

(FILE 'HOME' ENTERED AT 16:51:55 ON 25 MAY 2004)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:52:04 ON 25 MAY 2004

L1 0 S OX102  
L2 0 S OX 102  
L3 198 S OX2R OR OX2 RECEPTOR?  
L4 10 S L3 AND ANTIBOD?  
L5 7 DUP REM L4 (3 DUPLICATES REMOVED)  
L6 4401 S BARCLAY?IAU  
L7 12 S L3 AND L6

L8 8 DUP REM L7 (4 DUPLICATES REMOVED)  
L9 35 S CD200 (3A) RECEPTOR?  
L10 10 SL9 AND (ANTIBODY? OR MAB)  
L11 6 DUP REM L10 (4 DUPLICATES REMOVED)

=> s l3 or l9

L12 230 L3 OR L9

=> s l12 and mAb

L13 10 L12 AND MAB

=> dup rem l13

PROCESSING COMPLETED FOR L13

L14 4 DUP REM L13 (6 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 1

AN 2001:429194 BIOSIS

DN PREV200100429194

TI Transplant tolerance modifying antibody to \*\*\*CD200\*\*\*  
\*\*\*receptor\*\*\*, but not \*\*\*CD200\*\*\*, alters cytokine production  
profile from stimulated macrophages.

AU Gorczynski, Reginald M. [Reprint author]

CS Toronto Hospital, 200 Elizabeth Street, CCRW 2-855, Toronto, ON, M5G2C4,  
Canada

SO European Journal of Immunology, (August, 2001) Vol. 31, No. 8, pp.

2331-2337. print

CODEN: EJIMAF. ISSN: 0014-2980.

DT Article

LA English

ED Entered STN: 12 Sep 2001

Last Updated on STN: 22 Feb 2002

AB Increased C57BL/6 allograft survival following donor-specific dendritic  
cell (DC) portal vein (pv) pre-transplant immunization of C3H mice is  
associated with increased expression of the molecule CD200 on DC, delivery  
of suppressive signals by CD200+ macrophages, and polarization in  
cytokine production towards type-2 cytokines. Infusion of anti-mouse  
CD200 monoclonal antibody abolishes these effects. We have used whole Ig,  
and F(ab')2 fragments, of anti-CD200 and anti-CD200r \*\*\*mAb\*\*\* to  
explore the relative signaling role of CD200+ versus CD200r cells in  
suppression of type-1 cytokine production in mixed leukocyte cultures  
(MLC), and enhanced graft survival in vivo. Simple neutralization of  
CD200 (even by F(ab')2 antibody) reversed CD200-mediated suppression.  
However, only whole anti-CD200r antibody was effective in stimulating  
suppression from CD200r cells. Suppression of cytokine induction  
following cross-linking of CD200+ cells in vitro was attenuated by  
anti-IL-6 \*\*\*mAb\*\*\*. Our data are consistent with the hypothesis that  
CD200r itself delivers the crucial intracellular signal leading to  
immunosuppression, a feature likely of importance in autoimmunity and  
transplantation.

L14 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN

AN 2001:278650 BIOSIS

DN PREV200100278650

TI Role of MD-1 in regulation of alloimmunity and rejection.

AU Hadidi, Sima [Reprint author]; Gorczynski, Reginald [Reprint author]

CS University Health Network, 200 Elizabeth Str, CCRW2-855, Toronto, Ontario,  
M5G2C4, Canada

SO FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A342. print

Meeting Info.: Annual Meeting of the Federation of American Societies for  
Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA.  
March 31-April 04, 2001.

CODEN: FAJOEC. ISSN: 0892-6638.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 13 Jun 2001

Last Updated on STN: 19 Feb 2002

AB We have shown that after portal vein (pv) pre-transplant immunization,  
animals accept renal and skin allografts and xenografts longer than  
controls. Increased survival is associated with expression on dendritic  
cells (DCs) of a molecule, OX2, which we showed delivers a suppressive  
signal following interaction with its receptor, \*\*\*OX2R\*\*\*, on target  
cells. We also observed elevated expression of a molecule MD-1, which we  
hypothesized acted in opposition to OX2, controlling surface expression of  
CD80/CD86 which are implicated in rejection itself. We reported that  
incubation of DCs with anti-sense oligonucleotides (ODNs) to MD-1  
decreased expression of CD80/CD86 on those cells, and diminished their  
capacity to stimulate in vitro MLR and CTL reactions. We asked whether  
these ODNs were active in vivo in regulating graft rejection. C3H mice  
received multiple iv injections with anti-MD-1 (or control) ODNs following  
application of C57BL/6 skin allografts. Graft survival was followed 3  
mice/group were sacrificed at 12 days, spleen cells harvested and cells  
tested in vitro for allospecific and third-party immune responses (CTL  
induction: MLR proliferation; induction of IFN/IL-4 synthesis). Compared  
with control mice, anti-MD-1 treated animals showed >85% inhibition of  
alloimmunity in all assays, along with marked increases in IL-4 production  
and elevated graft survival. This was correlated with diminished MD-1

mRNA in tissue extracts from treated mice, with preservation of OX2  
expression. Finally we used rat \*\*\*mAb\*\*\* to murine MD-1 to assess an  
alternative means of inhibiting functional expression of MD-1 in vivo.  
Infusion of anti-MD-1 \*\*\*mAb\*\*\* into pv immunized mice further  
prolonged survival of allografts, and led to decreased allospecific immune  
responses from cells harvested from treated mice. Taken together, our  
data suggest that manipulations designed to decrease expression of MD-1,  
and increase that of OX2, synergize in decreasing rejection.

L14 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 2

AN 2001:187889 BIOSIS

DN PREV200100187889

TI The unusual distribution of the neuronal/lymphoid cell surface CD200 (OX2)  
glycoprotein is conserved in humans.

AU Wright, G. J.; Jones, M.; Puklavec, M. J.; Brown, M. H.; Barclay, A. N.

[Reprint author]

CS Sir William Dunn School of Pathology, South Parks Road, Oxford, OX1 3RE,  
UK

SO Immunology, (February, 2001) Vol. 102, No. 2, pp. 173-179. print

CODEN: IMMUAJ. ISSN: 0019-2805.

DT Article

LA English

ED Entered STN: 20 Apr 2001

Last Updated on STN: 18 Feb 2002

AB OX2 (CD200) is a type-1 membrane glycoprotein that contains two  
immunoglobulin superfamily domains and which is expressed on a variety of  
lymphoid and non-lymphoid cells in the rat. The recent characterization  
of a receptor for OX2 (\*\*\*OX2R\*\*\* ) on myeloid cells, and the phenotype  
of an OX2-deficient mouse, suggests that OX2 may regulate myeloid cell  
activity in anatomically diverse locations. Here we report the tissue  
distribution of the human homologue of the rat OX2 glycoprotein using a  
new monoclonal antibody (\*\*\*mAb\*\*\* ), OX104, raised against recombinant  
human OX2. Human OX2 was expressed at the cell surface of thymocytes, B  
cells, T cells, neurons, kidney glomeruli, tonsil follicles, the  
syncytiotrophoblast and endothelial cells. This broad, but not  
ubiquitous, distribution pattern is very similar to that observed in rats,  
suggesting that OX2 may regulate myeloid cell activity in a variety of  
tissues in humans.

L14 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 3

AN 2000:440556 BIOSIS

DN PREV200000440556

TI Lymphoid/neuronal cell surface OX2 glycoprotein recognizes a novel  
receptor on macrophages implicated in the control of their function.

AU Wright, Gavin J.; Puklavec, Michael J.; Willis, Antony C.; Hoek, Robert  
M.; Sedgwick, Jonathon D.; Brown, Marion H.; Barclay, A. Neil [Reprint  
author]

CS Sir William Dunn School of Pathology, University of Oxford, South Parks  
Road, Oxford, OX1 3RE, UK

SO Immunology, (August, 2000) Vol. 13, No. 2, pp. 233-242. print

ISSN: 1074-7613.

DT Article

LA English

OS Genbank-AF231392; Genbank-AF231393

ED Entered STN: 18 Oct 2000

Last Updated on STN: 10 Jan 2002

AB The OX2 membrane glycoprotein (CD200) is expressed on a broad range of  
tissues including lymphoid cells, neurons, and endothelium. We report the  
characterization of an \*\*\*OX2\*\*\* \*\*\*receptor\*\*\* (\*\*\*OX2R\*\*\* )  
that is a novel protein restricted to cells of the myeloid lineage. OX2  
and its receptor are both cell surface glycoproteins containing two  
immunoglobulin-like domains and interact with a dissociation constant of  
2.5 uM and koff 0.8 s-1, typical of many leukocyte protein membrane  
interactions. Pervanadate treatment of macrophages showed that  
\*\*\*OX2R\*\*\* could be phosphorylated on tyrosine residues. Blockade of  
the OX2- \*\*\*OX2R\*\*\* interaction with an \*\*\*OX2R\*\*\* \*\*\*mAb\*\*\*  
exacerbated the disease model experimental allergic encephalomyelitis.  
These data, together with data from an OX2-deficient mouse (R. M. Hoek  
et al., submitted), suggest that myeloid function can be controlled in a  
tissue-specific manner by the OX2- \*\*\*OX2R\*\*\* interaction.

=> s l12 and py<=1999

2 FILES SEARCHED..

L15 21 L12 AND PY<=1999

=> dup rem l15

PROCESSING COMPLETED FOR L15

L16 11 DUP REM L15 (10 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L16 ANSWER 1 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 1

AN 2000:37723 BIOSIS

DN PREV20000037723

TI Structure, tissue distribution, and pharmacological characterization of



- Xenopus orexins.
- AU Shibahara, Megumi; Sakurai, Takeshi [Reprint author]; Nambu, Tadahiro; Takenouchi, Takato; Iwaasa, Hisashi; Egashira, Shin-ichiro; Ihara, Masaki; Goto, Katsutoshi
- CS Institute of Basic Medical Sciences, University of Tsukuba, Tsukuba, Ibaraki, 305-8575, Japan
- SO Peptides (New York), (Oct., 1999) Vol. 20, No. 10, pp. 1169-1176. print. CODEN: PPTDD5. ISSN: 0196-9781.
- DT Article
- LA English
- ED Entered STN: 19 Jan 2000
- Last Updated on STN: 31 Dec 2001
- AB We isolated the Xenopus gene encoding prepro-orexin to predict the structures of orexins in submammalian chordates. Putative mature Xenopus orexin-A and -B are highly similar to each mammalian counterpart. Especially, the C-terminal 10 residues were highly conserved among these species and isopeptides. Immunohistochemical examination of Xenopus brain revealed that orexin-containing neurons were highly specifically localized in the ventral hypothalamic nucleus. A rich network of immunoreactive fibers was found in various regions of the Xenopus brain. The distribution was similar to that of mammalian orexins. Xenopus orexin-A and -B specifically bind and activate human orexin receptors expressed in Chinese hamster ovary cells. Of interest, Xenopus orexin-B had several-fold higher affinity to human \*\*\*OX2R\*\*\* compared with human orexins. These results suggest that Xenopus orexin-B might be a useful pharmacological tool as an \*\*\*OX2R\*\*\* selective high-affinity agonist.
- L16 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 1999:571534 CAPLUS
- DN 131:284870
- TI Narcolepsy in orexin knockout mice: molecular genetics of sleep regulation
- AU Chemelli, Richard M.; Willie, Jon T.; Sinton, Christopher M.; Elmquist, Joel K.; Scammell, Thomas; Lee, Charlotte; Richardson, James A.; Williams, S. Clay; Xiong, Yumei; Kisanuki, Yaz; Fitch, Thomas E.; Nakazato, Masamitsu; Hammer, Robert E.; Saper, Clifford B.; Yanagisawa, Masashi
- CS Howard Hughes Medical Institute Department of Molecular Genetics Department of Pediatrics, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75235-9050, USA
- SO Cell (Cambridge, Massachusetts) ( \*\*\*1999\*\*\* ), 98(4), 437-451
- CODEN: CELLB5; ISSN: 0092-8674
- PB Cell Press
- DT Journal
- LA English
- AB Neurons contg. the neuropeptide orexin (hypocretin) are located exclusively in the lateral hypothalamus and send axons to numerous regions throughout the central nervous system, including the major nuclei implicated in sleep regulation. Here, we report that, by behavioral and electroencephalog. criteria, orexin knockout mice exhibit a phenotype strikingly similar to human narcolepsy patients, as well as canarc-1 mutant dogs, the only known monogenic model of narcolepsy. Moreover, modafinil, an anti-narcoleptic drug with ill-defined mechanisms of action, activates orexin-contg. neurons. We propose that orexin regulates sleep/wakefulness states, and that orexin knockout mice are a model of human narcolepsy, a disorder characterized primarily by rapid eye movement (REM) sleep dysregulation.
- RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
- ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L16 ANSWER 3 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
- DUPLICATE 2
- AN 2000:154898 BIOSIS
- DN PREV200000154898
- TI Acute effects of orexins A and B on the rat pituitary-adrenocortical axis.
- AU Malendowicz, Ludwik K.; Tortorella, Cinzia; Nussdorfer, Gastone G. [Reprint author]
- CS Department of Human Anatomy and Physiology, Section of Anatomy, University of Padua, Padua, Italy
- SO Biomedical Research (Tokyo), (Oct., 1999) Vol. 20, No. 5, pp. 301-304. print. CODEN: BRES55. ISSN: 0388-6107.
- DT Article
- LA English
- ED Entered STN: 26 Apr 2000
- Last Updated on STN: 4 Jan 2002
- AB Orexins A and B are hypothalamic peptides, which act through two receptor subtypes, called OX1R and \*\*\*OX2R\*\*\*. They belong to a group of neuropeptides involved in the central regulation of food intake, members of which (neuropeptide Y and leptin) are known to modulate the function of the pituitary-adrenocortical axis (PAA). We examined the effects at 60 and 120 min of a subcutaneous injection of 5 or 10 nmol/kg of orexins on the function of the rat PAA. Orexin-A raised plasma concentrations of ACTH, aldosterone and corticosterone at both 60 and 120 min, corticosterone response being the most intense one. Orexin-B evoked a sizeable decrease in the plasma level of ACTH, without changing that of corticosterone. The effect of orexin-B on aldosterone plasma concentration was biphasic, the lower dose decreasing and the higher one increasing it at both 60 and 120 min. Evidence indicates that OX1R binds both orexins, while \*\*\*OX2R\*\*\* is selective for orexin-B, and that only \*\*\*OX2R\*\*\* is present in the hypothalamic nucleus paraventricularis. On these grounds, our findings allow us to conclude:
- (i) OX1R stimulates and \*\*\*OX2R\*\*\* inhibits rat PAA; (ii) orexin-A stimulates PAA, the activation of OX1R prevailing over that of \*\*\*OX2R\*\*\*, while orexin-B suppresses PAA function; and (iii) the aldosterone-secreting response to the higher dose of orexin-B may probably be ascribed to the activation of one or more extra-PAA mechanisms enhancing secretory activity of the zona glomerulosa.
- L16 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 1999:17219 CAPLUS
- DN 130:163414
- TI Distribution of orexin receptor mRNA in the rat brain. [Erratum to document cited in CA130:76402]
- AU Trivedi, Prashant; Yu, Hong; MacNeil, Douglas J.; Van der Ploeg, L. H. T.; Guan, Xiao-Ming
- CS Department of Obesity Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
- SO FEBS Letters ( \*\*\*1999\*\*\* ), 442(1), 122
- CODEN: FEBLAL; ISSN: 0014-5793
- PB Elsevier Science B.V.
- DT Journal
- LA English
- AB The second author was inadvertently not given the credit for having contributed equally to the study with the first author.
- L16 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 2000:264439 CAPLUS
- DN 133:26938
- TI Structure-activity relationship studies on the novel neuropeptide orexin
- AU Asahi, Shuichi; Egashira, Shin-ichiro; Matsuda, Masao; Iwaasa, Hisashi; Kanatani, Akio; Ohkubo, Mitsuru; Ihara, Masaki; Sakurai, Takeshi; Morishima, Hajime
- CS Banyu Tsukuba Research Institute in collaboration with Merck Research Laboratories, Tsukuba, 300-2611, Japan
- SO Peptide Science ( \*\*\*1999\*\*\* ), 36th, 37-40
- CODEN: PSCIFQ; ISSN: 1344-7661
- PB Japanese Peptide Society
- DT Journal
- LA English
- AB Orexins (also known as hypocretins) were recently identified as hypothalamic neuropeptides with various physiol. functions, including the regulation of feeding behavior. To characterize the structural requirements of orexin receptor selectivity, the authors conducted systematic structure-activity relationship studies on orexins. Peptide chain truncation, alanine scanning and D-amino acid scanning revealed that the entire sequence of orexin is not required for receptor activation, however the C-terminal region is crit. for agonistic activity.
- RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
- ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L16 ANSWER 6 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
- DUPLICATE 3
- AN 1999:477953 BIOSIS
- DN PREV199900477953
- TI Characterization of recombinant human orexin receptor pharmacology in a Chinese hamster ovary cell-line using FLIPR.
- AU Smart, D. [Reprint author]; Jerman, J. C.; Brough, S. J.; Rushton, S. L.; Murdock, P. R.; Jewitt, F.; Elshourbagy, N. A.; Ellis, C. E.; Middlemiss, D. N.; Brown, F.
- CS Neuroscience Research, New Frontiers Science Park, SmithKline Beecham Pharmaceuticals, Third Avenue, Harlow, Essex, CM19 5AW, UK
- SO British Journal of Pharmacology, (Sept., 1999) Vol. 128, No. 1, pp. 1-3. print. CODEN: BJPCBM. ISSN: 0007-1188.
- DT Article
- LA English
- ED Entered STN: 9 Nov 1999
- Last Updated on STN: 3 May 2000
- AB The cellular mechanisms underlying the physiological effects of the orexins are poorly understood. Therefore, the pharmacology of the recombinant human orexin receptors was studied using FLIPR. Intracellular calcium ((Ca2+)i) was monitored in Chinese hamster ovary (CHO) cells stably expressing orexin-1 (OX1) or orexin-2 (\*\*\*OX2\*\*\*). \*\*\*receptors\*\*\* using Fluo-3AM. Orexin-A and orexin-B increased (Ca2+)i in a concentration dependent manner in CHO-OX1 (pEC50 = 8.03 +/- 0.08 and 7.30 +/- 0.08 respectively, n = 5) and CHO-OX2 (pEC50 = 8.18 +/- 0.10 and 8.43 +/- 0.09 respectively, n = 5) cells. This response was typified as a rapid peak in (Ca2+)i (maximal at 6-8 s), followed by a gradually declining secondary phase. Thapsigargin (3 muM) or U73122 (3 muM) abolished the response. In calcium-free conditions the peak response was unaffected but the secondary phase was shortened, returning to basal values within 90 s. Calcium (1.5 mM) replacement restored the secondary phase. In conclusion, orexins cause a phospholipase C-mediated release of calcium from intracellular stores, with subsequent calcium influx.
- L16 ANSWER 7 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
- AN 1999:85722 BIOSIS
- DN PREV19990085722
- TI Distribution of orexin receptor mRNA in the rat brain.
- AU Trivedi, P.; Yu, H.; Macneil, D. J.; Van Der Ploeg, L. H. T.; Guan, X.-M.
- CS Dep. Obesity Res. Merck Res. Lab., Rahway, NJ 07065, USA

SO Society for Neuroscience Abstracts, (1998) Vol. 24, No. 1-2, pp. 2046.  
print.  
Meeting Info.: 28th Annual Meeting of the Society for Neuroscience, Part  
2. Los Angeles, California, USA. November 7-12, 1998. Society for  
Neuroscience.  
ISSN: 0190-5295.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)

LA English  
ED Entered STN: 1 Mar 1999  
Last Updated on STN: 1 Mar 1999

L16 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 4

AN 1999:5250 BIOSIS

DN PREV19990005250

TI Distribution of orexin receptor mRNA in the rat brain.

AU Trivedi, Prashant; Yu, Hong; Macneil, Douglas J.; Van Der Ploeg, L. H. T.;  
Guan, Xiao-Ming [Reprint author]

CS Dep. Obesity Res., Merck Res. Lab., P.O. Box 2000, R80M-213 Rahway, NJ  
07065, USA

SO FEBS Letters, (Oct. 30, 1998) Vol. 438, No. 1-2, pp. 71-75. print.  
CODEN: FEBLAL. ISSN: 0014-5793.

DT Article

LA English

ED Entered STN: 11 Jan 1999  
Last Updated on STN: 11 Jan 1999

AB The expression pattern of mRNA encoding two orexin receptors (OX1R and  
\*\*\*OX2R\*\*\* ) in the rat brain was examined. OX1R and \*\*\*OX2R\*\*\*  
exhibited marked differential distribution. Within the hypothalamus, OX1R  
mRNA is most abundant in the ventromedial hypothalamic nucleus whereas  
\*\*\*OX2R\*\*\* is predominantly expressed in the paraventricular nucleus.  
High levels of OX1R mRNA were also detected in tectal, the  
hippocampal formation, dorsal raphe, and locus coeruleus. \*\*\*OX2R\*\*\*  
mRNA is mainly expressed in cerebral cortex, nucleus accumbens,  
subthalamic and paraventricular thalamic nuclei, anterior pretectal  
nucleus. The presence of orexin receptor mRNA in the hypothalamus is in  
support of its proposed role in feeding regulation. Broad central  
distribution of orexin receptors may indicate additional functions for  
orexins.

L16 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1989:492495 CAPLUS

DN 111:92495

TI Receptor specificity of the Escherichia coli T-even type phage OX2.  
Mutational alterations in host range mutants

AU Drexler, Klaus; Riede, Isolde; Montag, Dirk; Eschbach, Marie Luise;  
Henning, Ulf

CS Max-Planck-Inst. Biol., Tuebingen, D-7400, Fed. Rep. Ger.

SO Journal of Molecular Biology ( \*\*\*1989\*\*\* ), 207(4), 797-803

CODEN: JMOBAK; ISSN: 0022-2836

DT Journal

LA English

AB The T-even type E. coli phage OX2 uses the outer membrane protein OmpA  
as

a receptor. The protein is recognized with the ends of the virion's long  
tail fibers. The 266 residue protein 38 is located at this site and acts  
as an adhesin. Host-range mutants had previously been isolated from OX2.  
Mutant OX2h5 is able to infect cells possessing an altered OmpA protein,  
which renders the cell resistant to OX2. OX2h10 was selected from OX2h5.  
This phage recognizes the OmpC protein in addn. to the OmpA protein.  
OX2h12, which stems from OX2h10, binds to OmpC with high affinity, but has  
lost efficient binding to OmpA. The mutational alterations caused in  
protein 38 are: Asp231.fwdarw. Asn(h5) and His170.fwdarw. Arg(h10). The  
triple mutant OX2h12 possesses an insertion of a Gly residue next to  
Gly121. The three mutants have addnl. acquired mutations affecting their  
base plate, making them "trigger-happy". When protein 38 was compared  
with the same protein derived from other E. coli phages, it was found to  
contain two const. and one variable domain, the latter harboring four  
hypervariable regions flanked by a largely conserved glycine-rich  
sequence. The h5 and h10 mutations occurred within two hypervariable  
areas, while the addnl. Gly residue was present in one of the flanking  
conserved sequences. On the basis of these results, as well as those  
obtained from host-range mutants analyzed previously, a model for such  
adhesins is proposed. Receptor recognition is most likely performed via  
the hypervariable regions, which may form loops held together in close  
proximity by the oligoglycine sequences. The latter may achieve this by  
being part of highly compact omega loops.

L16 ANSWER 10 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 5

AN 1985:238322 BIOSIS

DN PREV198579018318; BA79:18318

TI HOST RANGE MUTANTS OF BACTERIOPHAGE OX-2 CAN USE 2  
DIFFERENT OUTER

MEMBRANE PROTEINS OF ESCHERICHIA-COLI K-12 AS RECEPTORS.

AU MORONA R [Reprint author]; HENNING U

CS MAX-PLANCK-INSTITUT FUER BIOLOGIE, D-7400 TUEBINGEN, FRG

SO Journal of Bacteriology, (1984) Vol. 159, No. 2, pp. 579-582.

CODEN: JOBAAY. ISSN: 0021-9193.

DT Article

FS BA

LA ENGLISH

AB The E. coli K-12 outer membrane protein OmpA functions as the receptor for  
bacteriophage OX2. A host range mutant of this phage was isolated which  
was able to grow on an OX2-resistant ompA mutant producing an altered OmpA  
protein. From this mutant, OX2h5, a 2nd-step host range mutant was  
recovered which formed turbid plaques on a strain completely lacking the  
OmpA protein. From one of these mutants, OX2h10, a 3rd-step host range  
mutant, OX2h12, was isolated which formed clear plaques on a strain  
missing the OmpA protein. OX2h10 and OX2h12 apparently were able to use  
both outer membrane proteins OmpA and OmpC as receptors. Whereas the 2  
proteins are very different with respect to primary structures and  
functions, the OmpC protein is very closely related to another outer  
membrane protein, OmpF, which was not recognized by OX2h10 or OX2h12. An  
examination of the OmpC amino acid sequence, in the regions where it  
differs from that of OmpF, revealed that 1 region shares considerable  
homology with a region of the OmpA protein which most likely is required  
for phage \*\*\*OX2\*\*\* \*\*\*receptor\*\*\* activity.

L16 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1984:32130 CAPLUS

DN 100:32130

TI Role of lipopolysaccharide in the receptor function for bacteriophage OX2

AU Sukupolvi, Soila

CS Natl. Public Health Inst., Helsinki, Finland

SO FEMS Microbiology Letters ( \*\*\*1984\*\*\* ), 21(1), 83-7

CODEN: FMLED7; ISSN: 0378-1097

DT Journal

LA English

AB The sensitivity of Salmonella typhimurium as well as of Escherichia coli  
to bacteriophage OX2 required, in addn. to the OmpA protein, a certain  
type of rough lipopolysaccharide (LPS). Heptoseless mutants were  
resistant and unable to adsorb the phage. Mutants with less defective LPS  
chemotype were sensitive and could, except the 2nd most defective  
chemotypes, adsorb OX2. However, isolated LPS-free OmpA protein could  
bind the phage, and this binding could not be increased by adding LPS.

=> s l6 and (CD200 or CD 200)

L17 15 L6 AND (CD200 OR CD 200)

=> dup rem l17

PROCESSING COMPLETED FOR L17

L18 5 DUP REM L17 (10 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y(N):y

L18 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 1

AN 2003:539929 BIOSIS

DN PREV200300542479

TI Characterization of the \*\*\*CD200\*\*\* receptor family in mice and humans  
and their interactions with \*\*\*CD200\*\*\*

AU Wright, Gavin J.; Cherwinski, Holly; Foster-Cuevas, Mildred; Brooke, Gary;  
Puklavec, Michael J.; Bigler, Mike; Song, Yaoli; Jenmalm, Maria; Gorman,  
Dan; McClanahan, Terri; Liu, Man-ru; Brown, Marion H.; Sedgwick, Jonathan  
D.; Phillips, Joseph H.; \*\*\*Barclay, A. Neil\*\*\* [Reprint Author]

CS Sir William Dunn School of Pathology, University of Oxford, South Parks  
Road, Oxford, OX1 3RE, UK

joe.phillips@dnax.org; Neil.Barclay@path.ox.ac.uk

SO Journal of Immunology, (September 15 2003) Vol. 171, No. 6, pp. 3034-3046.  
print.

ISSN: 0022-1767 (ISSN print).

DT Article

LA English

ED Entered STN: 19 Nov 2003

Last Updated on STN: 19 Nov 2003

AB \*\*\*CD200\*\*\* (OX2) is a broadly distributed cell surface glycoprotein  
that interacts with a structurally related receptor (CD200R) expressed on  
rodent myeloid cells and is involved in regulation of macrophage function.  
We report the first characterization of human CD200R (hCD200R) and define  
its binding characteristics to hCD200. We also report the identification  
of a closely related gene to hCD200R, designated hCD200RLa, and four mouse  
CD200R-related genes (termed mCD200RLa-d). \*\*\*CD200\*\*\*, CD200R, and  
CD200R-related genes were closely linked in humans and mice, suggesting  
that these genes arose by gene duplication. The distributions of the  
receptor genes were determined by quantitative RT-PCR, and protein  
expression was confirmed by a set of novel mAbs. The distribution of  
mouse and human CD200R was similar, with strongest labeling of macrophages  
and neutrophils, but also other leukocytes, including monocytes, mast  
cells, and T lymphocytes. Two mCD200 receptor-like family members,  
designated mCD200RLa and mCD200RLb, were shown to pair with the  
activatory

adaptor protein, DAP12, suggesting that these receptors would transmit  
strong activating signals in contrast to the apparent inhibitory signal  
delivered by triggering the CD200R. Despite substantial sequence homology  
with mCD200R, mCD200RLa and mCD200RLb did not bind mCD200, and  
presently have unknown ligands. The \*\*\*CD200\*\*\* receptor gene family resembles  
the signal regulatory proteins and killer Ig-related receptors in having



receptor family members with potential activatory and inhibitory functions that may play important roles in immune regulation and balance. Because manipulation of the \*\*\*CD200\*\*\*-CD200R interaction affects the outcome of rodent disease models, targeting of this pathway may have therapeutic utility.

L18 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 2

AN 2002:352369 BIOSIS

DN PREV200200352369

TI \*\*\*CD200\*\*\* and membrane protein interactions in the control of myeloid cells.

AU \*\*\*Barclay, A. Neil\*\*\* [Reprint author]; Wright, Gavin J.; Brooke, Gary [Reprint author]; Brown, Marion H. [Reprint author]

CS Sir William Dunn School of Pathology, University of Oxford, Oxford, OX1 3RE, UK

barclay@molbiol.ox.ac.uk

SO Trends in Immunology, (June, 2002) Vol. 23, No. 6, pp. 285-290. print. ISSN: 1471-4906.

DT Article

LA English

ED Entered STN: 26 Jun 2002

Last Updated on STN: 26 Jun 2002

AB OX2 (now designated \*\*\*CD200\*\*\*) is a membrane protein expressed by a broad range of cell types. It is the ligand for a receptor restricted to myeloid cells, with the potential to deliver inhibitory signals. This is indicated by the \*\*\*CD200\*\*\*-deficient mouse model, in which myeloid cells are more activated when stimulated immunologically than cells from normal mice. The unusual tissue distribution of \*\*\*CD200\*\*\* indicates where myeloid cells can be restrictively controlled through cell-cell contact. Recent data on \*\*\*CD200\*\*\* will be reviewed in the context of other proteins that might have similar roles, in particular, the interaction between CD47 and SIRPalpha (CD172a).

L18 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 3

AN 2001:187889 BIOSIS

DN PREV200100187889

TI The unusual distribution of the neuronal/lymphoid cell surface \*\*\*CD200\*\*\* (OX2) glycoprotein is conserved in humans.

AU Wright, G. J.; Jones, M.; Puklavec, M. J.; Brown, M. H.; \*\*\*Barclay, A.\*\*\* [Reprint author]

CS Sir William Dunn School of Pathology, South Parks Road, Oxford, OX1 3RE, UK

SO Immunology, (February, 2001) Vol. 102, No. 2, pp. 173-179. print. CODEN: IMMUA. ISSN: 0019-2805.

DT Article

LA English

ED Entered STN: 20 Apr 2001

Last Updated on STN: 18 Feb 2002

AB OX2 (\*\*\*CD200\*\*\*) is a type-1 membrane glycoprotein that contains two immunoglobulin superfamily domains and which is expressed on a variety of lymphoid and non-lymphoid cells in the rat. The recent characterization of a receptor for OX2 (OX2R) on myeloid cells, and the phenotype of an OX2-deficient mouse, suggests that OX2 may regulate myeloid cell activity in anatomically diverse locations. Here we report the tissue distribution of the human homologue of the rat OX2 glycoprotein using a new monoclonal antibody (mAb), OX104, raised against recombinant human OX2. Human OX2 was expressed at the cell surface of thymocytes, B cells, T cells, neurons, kidney glomeruli, tonsil follicles, the syncytiotrophoblast and endothelial cells. This broad, but not ubiquitous, distribution pattern is very similar to that observed in rats, suggesting that OX2 may regulate myeloid cell activity in a variety of tissues in humans.

L18 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 4

AN 2001:44456 BIOSIS

DN PREV200100044456

TI Down-regulation of the macrophage lineage through interaction with OX2 (\*\*\*CD200\*\*\*).

AU Hoek, Robert M.; Ruuls, Sigrid R.; Murphy, Craig A.; Wright, Gavin J.; Goddard, Ruth; Zurawski, Sandra M.; Blom, Bianca; Homola, Margit E.; Streit, Wolfgang J.; Brown, Marion H.; \*\*\*Barclay, A. Neil\*\*\*; Sedgwick, Jonathan D. [Reprint author]

CS DNAX Research Institute of Molecular and Cellular Biology, 901 California Avenue, Palo Alto, CA, 94304, USA

jon.sedgwick@dnax.org

SO Science (Washington D C), (1 December, 2000) Vol. 280, No. 5497, pp. 1768-1771. print. CODEN: SCIEAS. ISSN: 0036-8075.

DT Article

General Review; (Literature Review)

LA English

ED Entered STN: 17 Jan 2001

Last Updated on STN: 12 Feb 2002

AB OX2 (\*\*\*CD200\*\*\*) is a broadly expressed membrane glycoprotein, shown here to be important for regulation of the macrophage lineage. In mice lacking \*\*\*CD200\*\*\*, macrophage lineage cells, including brain microglia, exhibited an activated phenotype and were more numerous. Upon facial nerve transection, damaged \*\*\*CD200\*\*\*-deficient neurons

elicited an accelerated microglial response. Lack of \*\*\*CD200\*\*\* resulted in a more rapid onset of experimental autoimmune encephalomyelitis (EAE). Outside the brain, disruption of \*\*\*CD200\*\*\*-\*\*\*CD200\*\*\* receptor interaction precipitated susceptibility to collagen-induced arthritis (CIA) in mice normally resistant to this disease. Thus, in diverse tissues OX2 delivers an inhibitory signal for the macrophage lineage.

L18 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 5

AN 2000:440556 BIOSIS

DN PREV200000440556

TI Lymphoid/neuronal cell surface OX2 glycoprotein recognizes a novel receptor on macrophages implicated in the control of their function.

AU Wright, Gavin J.; Puklavec, Michael J.; Willis, Antony C.; Hoek, Robert M.; Sedgwick, Jonathan D.; Brown, Marion H.; \*\*\*Barclay, A. Neil\*\*\* [Reprint author]

CS Sir William Dunn School of Pathology, University of Oxford, South Parks Road, Oxford, OX1 3RE, UK

SO Immunity, (August, 2000) Vol. 13, No. 2, pp. 233-242. print. ISSN: 1074-7613.

DT Article

LA English

OS Genbank-AF231392; Genbank-AF231393

ED Entered STN: 18 Oct 2000

Last Updated on STN: 10 Jan 2002

AB The OX2 membrane glycoprotein (\*\*\*CD200\*\*\*) is expressed on a broad range of tissues including lymphoid cells, neurons, and endothelium. We report the characterization of an OX2 receptor (OX2R) that is a novel protein restricted to cells of the myeloid lineage. OX2 and its receptor are both cell surface glycoproteins containing two immunoglobulin-like domains and interact with a dissociation constant of 2.5 muM and koff 0.8 s-1, typical of many leukocyte protein membrane interactions. Pervanadate treatment of macrophages showed that OX2R could be phosphorylated on tyrosine residues. Blockade of the OX2-OX2R interaction with an OX2R mAb exacerbated the disease model experimental allergic encephalomyelitis. These data, together with data from an OX2-deficient mouse (R. M. Hoek et al., submitted), suggest that myeloid function can be controlled in a tissue-specific manner by the OX2-OX2R interaction.

=> s CD200R

L19 38 CD200R

=> dup rem l19

PROCESSING COMPLETED FOR L19

L20 22 DUP REM L19 (16 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 22 ANSWERS - CONTINUE? Y(N):y

L20 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:757548 CAPLUS

DN 139:275741

TI Antibodies, agonists and antagonists to CD200 receptors for diagnosis and treatment of immune disease, inflammation, infection and cancer

IN Cherwinski, Holly M.; Phillips, Joseph H.; Sedgwick, Jonathan D.; Bigler, Michael E.; Murphy, Craig A.

PA Schering Corporation, USA

SO PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003077947	A1	20030925	WO 2003-US7647	20030313

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003223991 A1 20031204 US 2003-389231 20030313

PRAI US 2002-364513P P 20020315

AB Abstr. Provided are methods for modulating activity of the immune system using agonists or antagonists of a CD200 receptor. The agonists or antagonists are humanized antibodies, monoclonal antibodies, polyclonal antibodies, antibody fragments, peptide mimetic of antibody. The antibodies, agonists and antagonists are provided for treatment and diagnosis of immune and autoimmune disorder, inflammation, rheumatoid arthritis, endotoxemia, psoriasis, allergy, infection or cancer.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 1  
 AN 2003:539929 BIOSIS  
 DN PREV200300542479  
 TI Characterization of the CD200 receptor family in mice and humans and their interactions with CD200.  
 AU Wright, Gavin J.; Cherwinski, Holly; Foster-Cuevas, Mildred; Brooke, Gary; Puklavec, Michael J.; Bigler, Mike; Song, Yaoli; Jenmalm, Maria; Gorman, Dan; McClanahan, Terri; Liu, Man-ru; Brown, Marion H.; Sedgwick, Jonathon D.; Phillips, Joseph H.; Barclay, A. Neil [Reprint Author]  
 CS Sir William Dunn School of Pathology, University of Oxford, South Parks Road, Oxford, OX1 3RE, UK  
 joe.phillips@dnax.org; Neil.B Barclay@path.ox.ac.uk  
 SO Journal of Immunology, (September 15 2003) Vol. 171, No. 6, pp. 3034-3046.  
 print.  
 ISSN: 0022-1767 (ISSN print).

DT Article  
 LA English  
 ED Entered STN: 19 Nov 2003  
 Last Updated on STN: 19 Nov 2003

AB CD200 (OX2) is a broadly distributed cell surface glycoprotein that interacts with a structurally related receptor (\*\*\*CD200R\*\*\*) expressed on rodent myeloid cells and is involved in regulation of macrophage function. We report the first characterization of human CD200R (hCD200R) and define its binding characteristics to hCD200. We also report the identification of a closely related gene to hCD200R, designated hCD200RLa, and four mouse CD200R-related genes (termed mCD200RLa-d). CD200, \*\*\*CD200R\*\*\*, and \*\*\*CD200R\*\*\*-related genes were closely linked in humans and mice, suggesting that these genes arose by gene duplication. The distributions of the receptor genes were determined by quantitative RT-PCR, and protein expression was confirmed by a set of novel mAbs. The distribution of mouse and human \*\*\*CD200R\*\*\* was similar, with strongest labeling of macrophages and neutrophils, but also other leukocytes, including monocytes, mast cells, and T lymphocytes. Two mCD200 receptor-like family members, designated mCD200RLa and mCD200RLb, were shown to pair with the activatory adaptor protein, DAP12, suggesting that these receptors would transmit strong activating signals in contrast to the apparent inhibitory signal delivered by triggering the \*\*\*CD200R\*\*\*. Despite substantial sequence homology with mCD200R, mCD200RLa and mCD200RLb did not bind mCD200, and presently have unknown ligands. The CD200 receptor gene family resembles the signal regulatory proteins and killer Ig-related receptors in having receptor family members with potential activatory and inhibitory functions that may play important roles in immune regulation and balance. Because manipulation of the CD200-\*\*\*CD200R\*\*\* interaction affects the outcome of rodent disease models, targeting of this pathway may have therapeutic utility.

L20 ANSWER 3 OF 22 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN

DUPLICATE 2  
 AN 2003214539 EMBASE  
 TI Modulation of CD200 receptors as a novel method of immunosuppression.  
 SO Expert Opinion on Therapeutic Patents, (1 May 2003) 13/5 (711-715).  
 Refs: 34  
 ISSN: 1354-3776 CODEN: EOTPEG  
 CY United Kingdom  
 DT Journal; Article  
 FS 022 Human Genetics  
 026 Immunology, Serology and Transplantation  
 029 Clinical Biochemistry  
 030 Pharmacology  
 037 Drug Literature Index  
 LA English  
 SL English

AB Current methods of therapeutic immunomodulation are unsatisfactory. More effective and safer strategies are needed either to suppress immune responses for the treatment of transplant rejections, autoimmunity and allergy or to boost immunity against infectious diseases and cancer. This patent application proposes a novel approach towards these goals based on targeting CD200 receptors (\*\*\*CD200R\*\*\*). Whereas CD200 is expressed on lymphoid cells, neurons and endothelium, \*\*\*CD200R\*\*\* are mainly expressed on macrophages and myeloid cells. Crosslinking \*\*\*CD200R\*\*\* with CD200-Fc, an immunoadhesin made up of the CD200 extracellular region fused to the murine IgG2a Fc region or with anti-\*\*\*CD200R\*\*\* monoclonal antibodies (mAbs) can prolong allograft and xenograft survival and ameliorate collagen-induced arthritis in mice. Murine \*\*\*CD200R\*\*\* isoforms were identified by genomic analyses and partially characterised using specific mAbs acting presumably as receptor agonists. Myeloid dendritic cells (DCs) generated in the presence of anti-\*\*\*CD200R\*\*\* isoform mAbs were unable to stimulate the production of IFN-gamma, and cytolytic lymphocytes in a mixed lymphocyte culture but induced the emergence of suppressor cells. When injected prior to transplantation, such DCs were capable of significantly prolonging skin allograft survival. Although the data suggest that \*\*\*CD200R\*\*\* might serve to dampen immune responses, further investigations are required to determine whether this approach would be applicable to human disease situations.

L20 ANSWER 4 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
 DUPLICATE 3  
 AN 2003:408966 BIOSIS  
 DN PREV200300408966

TI Control of myeloid activity during retinal inflammation.  
 AU Dick, Andrew D. [Reprint Author]; Carter, Debra; Robertson, Morag; Broderick, Cathryn; Hughes, Edward; Forrester, John V.; Liversidge, Janet  
 CS Division of Ophthalmology, University of Bristol, Bristol Eye Hospital, Lower Maudlin Street, Bristol, BS1 2LX, UK  
 a.dick@Bristol.ac.uk  
 SO Journal of Leukocyte Biology, (August 2003) Vol. 74, No. 2, pp. 161-166.  
 print.  
 ISSN: 0741-5400 (ISSN print).

DT Article  
 General Review; (Literature Review)  
 LA English  
 ED Entered STN: 3 Sep 2003  
 Last Updated on STN: 3 Sep 2003

AB Combating myeloid cell-mediated destruction of the retina during inflammation or neurodegeneration is dependent on the integrity of homeostatic mechanisms within the tissue that may suppress T cell activation and their subsequent cytokine responses, modulate infiltrating macrophage activation, and facilitate healthy tissue repair. Success is dependent on response of the resident myeloid-cell populations (microglia (MG)) to activation signals, commonly cytokines, and the control of infiltrating macrophage activation during inflammation, both of which appear highly programmed in normal and inflamed retina. The evidence that tissue CD200 constitutively provides down-regulatory signals to myeloid-derived cells via cognate CD200-CD200 receptor (R) interaction supports inherent tissue control of myeloid cell activation. In the retina, there is extensive neuronal and endothelial expression of CD200. Retinal MG in CD200 knockout mice display normal morphology but unlike the wild-type mice, are present in increased numbers and express nitric oxide synthase 2, a macrophage activation marker, inferring that loss of CD200 or absent \*\*\*CD200R\*\*\* ligation results in "classical" activation of myeloid cells. Thus, when mice lack CD200, they show increased susceptibility to and accelerated onset of tissue-specific autoimmunity.

L20 ANSWER 5 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 4  
 AN 2003:442827 BIOSIS  
 DN PREV200300442827  
 TI Characterization of human cd200 glycoprotein receptor gene located on chromosome 3q12-13.  
 AU Vieites, Jose Maria; de la Torre, Raul; Ortega, Maria Angeles; Montero, Trinidad; Peco, Jose Maria; Sanchez-Pozo, Antonio; Gil, Angel; Suarez, Antonio [Reprint Author]  
 CS Department of Biochemistry and Molecular Biology, University of Granada, 18071, Granada, Spain  
 asuarez@ugr.es  
 SO Gene (Amsterdam), (5 June 2003) Vol. 311, pp. 99-104. print.  
 ISSN: 0378-1119 (ISSN print).

DT Article  
 LA English  
 ED Entered STN: 24 Sep 2003  
 Last Updated on STN: 24 Sep 2003

AB An immunomodulatory membrane protein, \*\*\*CD200R\*\*\* displays an expression pattern restricted to myeloid cells in mice. It is the receptor for a ligand, CD200, expressed by a broad range of cell types. In this study, we describe the cloning and characterization of the human homologue of the \*\*\*CD200R\*\*\* gene. This gene maps closely to the CD200 gene on human chromosome 3q12-13. The human \*\*\*CD200R\*\*\* gene spans a region of 52 kb, consists of nine exons, and encodes a 348-amino-acid cell-surface protein consisting of two IgFF domains in a typical V/C2 arrangement. The 59-amino-acid cytoplasmic domain has two tyrosine residues, one of which is contained within a NPXY motif. In common with other IgSF genes, the \*\*\*CD200R\*\*\* gene can generate different protein isoforms through alternative splicing. An alternative spliceout form, which has not yet been described in mice, encodes a 188-amino-acid truncated soluble polypeptide containing only the V immunoglobulin domain. In contrast to murine \*\*\*CD200R\*\*\* protein, the human membrane-bound and soluble \*\*\*CD200R\*\*\* proteins have an insertion of 23 amino acids at position 23, encoded by exon 2, which generates a putative dihydroxyacid dehydratase domain. The splicing of exon 2 generates two new isoforms, encoding the membrane and soluble proteins but lacking the dihydroxyacid dehydratase domain. Northern-blot analysis shows that both membrane-bound and soluble isoforms are expressed in the thymus, liver, spleen and placenta. By RT-PCR, we have analyzed the expression of the four transcript variants in human placenta, spleen, liver, brain and kidney.

L20 ANSWER 6 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2004:64670 BIOSIS  
 DN PREV20040062713  
 TI Structural and functional heterogeneity in the \*\*\*CD200R\*\*\* family of immunoregulatory molecules.  
 AU Lee, Lydia [Reprint Author]; Chen, Zhiqi [Reprint Author]; Wong, Simon; YuKai, Gary [Reprint Author]; Marsden, Philip A.; Gorczynski, Reginald M. [Reprint Author]  
 CS Transplant Division, Toronto General Hospital, 200 Elizabeth St, Toronto, ON, M5G 2C4, Canada  
 SO FASEB Journal, (April 14 2003) Vol. 17, No. 7, pp. C63. print.  
 Meeting Info.: 90th Anniversary Annual Meeting of the American Association of Immunologists. Denver, CO, USA. May 06-10, 2003. American Association

of Immunologists.  
ISSN: 0892-6638 (ISSN print).  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 28 Jan 2004  
Last Updated on STN: 28 Jan 2004

L20 ANSWER 7 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN  
AN 2004:181049 BIOSIS  
DN PREV200400181031  
TI CD200 is a novel p53-target gene involved in apoptosis-associated immune  
tolerance.

AU Rosenblum, Michael D. [Reprint Author]; Olsasz, Edit; Woodliff, Jeffrey E.  
[Reprint Author]; Johnson, Bryon D. [Reprint Author]; Orentas, Rimas J.  
[Reprint Author]; Truitt, Robert L. [Reprint Author]  
CS Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI, USA  
SO Blood, (November 16 2003) Vol. 102, No. 11, pp. 47a-48a. print  
Meeting Info.: 45th Annual Meeting of the American Society of Hematology.  
San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 7 Apr 2004  
Last Updated on STN: 7 Apr 2004

AB During apoptotic cell death, biochemical processes modify self-proteins  
and create potential autoantigens. To maintain self-tolerance in the face  
of natural cell turnover, the immune system must prevent or control  
responses to apoptosis-associated autoantigens or risk autoimmunity. The  
molecular mechanisms governing this process remain largely unknown. CD200  
is a transmembrane glycoprotein that imparts a negative immunoregulatory  
signal through its receptor ( \*\*\*CD200R\*\*\* ). We observed increased  
CD200 expression on CD11c+ dendritic cells (DCs) that were undergoing  
apoptosis in vivo. Since apoptotic DCs are thought to play a central role  
in the establishment and maintenance of peripheral tolerance to  
self-antigens, we sought to confirm that CD200 expression increases as DCs  
undergo apoptosis and determine whether CD200 on apoptotic DCs plays a  
role in the induction of immune tolerance. We used a model in which DCs  
spontaneously undergo apoptosis when cultured in the absence of growth  
factors to examine CD200 expression over time. Both CD200 mRNA and cell  
surface expression increased as splenic DCs underwent apoptosis. In  
quantitative real-time PCR assays, we observed >8-fold increases in CD200  
mRNA after 24hrs of culture when approximately 70% of DCs were apoptotic.  
Sorting cultured DCs into Annexin V+ and Annexin V- subsets revealed  
expression of CD200 on Annexin V+ DCs to be >20X that of Annexin V- DCs.  
We next explored mechanisms that might be involved in the control of CD200  
expression during apoptosis. p53 has been coined the "master regulator" of  
apoptosis because of its role in many of the signaling pathways initiated  
in apoptotic cells. p53 acts primarily as a DNA sequence-specific  
transcription factor. Sequence analysis revealed p53-response elements in  
both murine and human CD200 genes. We defined CD200 as a p53-target  
gene

using an in vitro luciferase-reporter assay and by kinetic analysis of  
CD200 expression on DCs isolated from p53-/- mice. CD200 expression was  
significantly diminished in apoptotic DCs isolated from p53-/- mice;  
however, we detected a caspase-dependent, p53-independent pathway that led  
to CD200 expression in p53-deficient DCs. We used autologous mixed  
lymphocyte reaction (MLR) cultures to examine the effect of CD200 on the  
CD4-mediated T cell response to caspase-generated autoantigens. CD200 on  
apoptotic DCs (vs. CD200-/- DCs) significantly diminished  
pro-inflammatory cytokines (IFNgamma and TNFalpha) in autologous MLR  
cultures, but not IL-2 production or T cell proliferation. Finally, we  
examined the effect of CD200 on induction of immune tolerance in vivo  
using a well-characterized system of UVB-induced immunosuppression of  
contact hypersensitivity that is dependent on apoptotic DCs. CD200 was  
essential for induction of immune tolerance to haptenated self-proteins in  
this assay. Our data suggest that CD200-mediated signaling is a novel  
molecular mechanism whereby apoptotic DCs suppress reactivity to  
apoptosis-associated autoantigens and maintain peripheral tolerance in the  
steady state.

L20 ANSWER 8 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN  
AN 2003:514807 BIOSIS  
DN PREV200300511752

TI LACKING CD200 DOES NOT IMPAIR MACROPHAGE ABILITY TO  
RESPOND TO TGFbeta  
DESPITE ACTIVATION AND HIGH NITRITE PRODUCTION IN STEADY -  
STATE.

AU Banerjee, D. [Reprint Author]; Sedgwick, J. D.; Nicholls, S. [Reprint  
Author]; Dick, A. D. [Reprint Author]  
CS Division of Ophthalmology, University of Bristol, Bristol, UK  
SO ARVO Annual Meeting Abstract Search and Program Planner, (2003) Vol.  
2003,

pp. Abstract No. 725. cd-rom.  
Meeting Info.: Annual Meeting of the Association for Research in Vision  
and Ophthalmology. Fort Lauderdale, FL, USA. May 04-08, 2003. Association  
for Research in Vision and Ophthalmology.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English

ED Entered STN: 5 Nov 2003  
Last Updated on STN: 5 Nov 2003

AB Purpose: Macrophage activation and conditioning during inflammation is  
dependent upon initial cytokine stimulation. Recent evidence of cognate  
suppression of macrophage activation via the CD200 receptor ( \*\*\*CD200R\*\*\* ) following CD200 engagement is supported by studies in  
CD200KO mice which display increased susceptibility to and early onset of  
experimental autoimmunity. We therefore wished to investigate if in the  
absence of CD200, macrophages remain responsive to further cytokine  
programming, which may be adapted therapeutically to suppress tissue  
damage. Methods: Experimental autoimmune uveoretinitis (EAU) was induced  
in CD200-/- (KO) and C57BL/6 Wild type (WT) mice following immunisation  
with IRBP-1-20 peptide with adjuvant. At days 15,25,32 post immunisation,  
retinal macrophages were isolated and function and ability to respond to  
cytokines was assessed via nitrite production, NOS2 expression and  
beta-glucuronidase expression with or without further cytokine stimulation  
in vitro. Results: In the absence of CD200, retinal macrophages have  
increased nitrite production, but nitrite production at height of disease,  
and their ability to respond to IFNgamma and TNF-mediated nitrite  
production is reduced compared to WT. In KO mice, macrophages still  
respond to TGFbeta-mediated suppression of nitrite production and are  
enabled to express beta-glucuronidase during resolution of disease.  
Conclusions: Loss of CD200 expression releases tonic macrophage  
suppression, as seen by increased NOS2 and nitrite production in the  
steady state, but macrophages do not respond to further cytokine-mediated  
nitrite production. CD200 did not regulate TGFbeta-mediated macrophage  
conditioning which may explain the ability to resolve inflammation despite  
constitutive macrophage activation.

L20 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2002:906505 CAPLUS  
DN 138:12292

TI Cloning and characterization of mouse CD200 receptor variants, and  
therapeutic use thereof in modulating immune response in animal  
transplantation and immune diseases  
IN Gorczynski, Reginald M.; Marsden, Philip  
PA Transplantation Technologies Inc., Can.; Trillium Therapeutics Inc.  
SO PCT Int. Appl., 189 pp.  
CODEN: PIXXD2

DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002095030	A2	20021128	WO 2002-CA734	20020524
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WO 2002095030	A3	20030821		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2001-292950P P 20010524  
US 2002-369862P P 20020405

AB The present invention relates to CD200 receptor isoforms and modulators thereof and their use in methods of immune modulation and pharmaceutical compns. In particular, protein and cDNA sequences for three isoforms of the murine CD200 receptor called CD200R2a, CD200R2b and CD200R3a are provided. The inventors have also prepd. antibodies to the different isoforms of \*\*\*CD200R\*\*\*. Studies of using \*\*\*CD200R\*\*\* antibodies, co-administering the CD200 receptor with a CD200 peptide, preferably in the form of a sol. fusion protein, such as CD200:Fc, to modulate immune response are presented. The inventors have also shown that administering antibody fragments [e.g. Fab or F(ab')2 fragments] that bind to a CD200 receptor inhibits the immune suppression caused by CD200. Accordingly, in another aspect, the present invention provides a method of inhibiting immune suppression by administering an effective amt. of a CD200 receptor antagonist to a cell or animal in need thereof. Preferably, the antagonist is an agent that inhibits the interaction of the CD200 receptor with CD200.

L20 ANSWER 10 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 5  
AN 2002:425169 BIOSIS  
DN PREV200200425169

TI A CD200Fc immunoadhesin prolongs rat islet xenograft survival in mice.  
AU Gorczynski, R. M. [Reprint author]; Hu, J.; Chen, Z.; Kai, Y.; Lei, J.  
CS Toronto Hospital, 200 Elizabeth Street, CCRW 2-855, Toronto, ON, M5G2C4, Canada

SO Transplantation (Baltimore), (June 27, 2002) Vol. 73, No. 12, pp.  
1948-1953. print  
CODEN: TRPLAU. ISSN: 0041-1337.

DT Article  
LA English  
ED Entered STN: 7 Aug 2002  
Last Updated on STN: 7 Aug 2002

AB Background: A solubilized form of the CD200 molecule, CD200Fc, has been shown to suppress allograft rejection and development of collagen-induced

arthritis in mice. We investigated whether the same molecule could prolong survival of rat islet xenografts. Methods: Streptozocin-treated mice, receiving injections with anti-asialo-GM1 antibody, received rat islets (approx 400/mouse) under the kidney capsule or injected into the portal vein, along with rapamycin treatment. Thereafter mice received injections of CD200Fc (10 mug/mouse/injection) or control mouse IgG2. Blood glucose was monitored daily. Some mice received additional injections of anti-CD200/- \*\*\*CD200R\*\*\* monoclonal antibodies. Results: Portal vein delivery of islets led to more extended resolution of diabetes than did transplantation under the kidney capsule. CD200Fc further prolonged survival in either case, an effect abolished by anti-CD200 or F(ab')2 anti- \*\*\*CD200R\*\*\* mAbs, but not by whole anti- \*\*\*CD200R\*\*\* (anti- \*\*\*CD200R\*\*\* Ig). Spleen cells taken from CD200Fc-treated mice showed polarization to type-2 cytokine production (interleukin-4, interleukin-10) on restimulation with rat splenocytes in culture, in comparison to cells from control mice (type-1 cytokines, interleukin-2, interferon-gamma). Conclusion: CD200/- \*\*\*CD200R\*\*\* interactions are important in regulating rat islet xenograft survival.

L20 ANSWER 11 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 6

AN 2002:614737 BIOSIS

DN PREV200200614737

TI Constitutive retinal CD200 expression regulates resident microglia and activation state of inflammatory cells during experimental autoimmune uveoretinitis.

AU Broderick, Cathryn; Hoek, Robert M.; Forrester, John V.; Liversidge, Janet; Sedgwick, Jonathan D.; Dick, Andrew D. [Reprint author]

CS Division of Ophthalmology, Bristol Eye Hospital, Lower Maudlin St, Bristol, BS1 2LX, UK  
a.dick@bristol.ac.uk

SO American Journal of Pathology, (November, 2002) Vol. 161, No. 5, pp. 1669-1677. print.

CODEN: AJPA44. ISSN: 0002-9440.

DT Article

LA English

ED Entered STN: 4 Dec 2002

Last Updated on STN: 4 Dec 2002

AB Recent evidence supports the notion that tissue OX2 (CD200) constitutively provides down-regulatory signals to myeloid-lineage cells via CD200-receptor ( \*\*\*CD200R\*\*\* ). Thus, mice lacking CD200 (CD200-/-) show increased susceptibility to and accelerated onset of tissue-specific autoimmunity. In the retina there is extensive expression of CD200 on neurons and retinal vascular endothelium. We show here that retinal microglia in CD200-/- mice display normal morphology, but unlike microglia from wild-type CD200+/+ mice are present in increased numbers and most significantly, express inducible nitric oxide synthase (NOS2), a macrophage activation marker. Onset and severity of uveitogenic peptide (1-20) of interphotoreceptor retinoid-binding protein-induced experimental autoimmune uveoretinitis is accelerated in CD200-/- mice and although tissue destruction appears no greater than seen in CD200+/+ mice, there is continued increased ganglion and photoreceptor cell apoptosis. Myeloid cell infiltrate was increased in CD200-/- mice during experimental autoimmune uveoretinitis, although NOS2 expression was not heightened. The results indicate that the CD200/- \*\*\*CD200R\*\*\* axis regulates retinal microglial activation. In CD200-/- mice the release of suppression of tonic macrophage activation, supported by increased NOS2 expression in the CD200-/- steady state accelerates disease onset but without any demonstration of increased target organ/tissue destruction.

L20 ANSWER 12 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2002:370490 BIOSIS

DN PREV200200370490

TI CD200Fc and anti- \*\*\*CD200R\*\*\* regulates collagen induced arthritis (CIA) in mice.

AU Gorczynski, Reginald M. [Reprint author]; Chen, Zhiqi [Reprint author]; Hu, Jiang [Reprint author]; Lee, Lydia [Reprint author]; Manuel, Justin [Reprint author]; Kai, Yu [Reprint author]

CS Transplant Research Division, Toronto Hospital, 200 Elizabeth Street, CCRW 2-855, Toronto, ON, M5G2C4, Canada

SO FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1045. print.  
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.  
CODEN: FAJOEC. ISSN: 0892-6638.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 3 Jul 2002

Last Updated on STN: 3 Jul 2002

AB Introduction: DBA/1 mice immunized with bovine collagen type-II in Complete Freund's Adjuvant (CFA), followed by boost in ICF, develop arthritis (>22/30 mice) by 30 days. The relatively ubiquitously expressed molecule CD200 is implicated in immunosuppression, and the immunoadhesin CD200Fc blocks graft rejection. We asked whether CD200Fc regulates CIA. Methods: DBA/1 mice received CD200Fc at 3 day intervals after collagen immunization. Disease was monitored daily. Serum was sampled for cytokines and anti-collagen immunoglobulin. Spleen cells were assayed for anti-collagen responses on restimulation. Results: CD200Fc treated mice did not develop arthritis. Cells from CD200Fc treated mice produced less TNF and IFN in culture supernatants after restimulation in vitro than those from control (normal immunoglobulin, Ig) treated mice. Serum from

CD200Fc mice contained less anti-collagen IgG, with more IgG2b and IgG3, and less TNF and IFN, than control mice. Similar regulation of disease induction was seen using anti-CD200 receptor Ig, which is believed to transmit intracellular (suppressive) signals following CD200 engagement. Conclusion: Immunotherapy with CD200Fc may regulate autoimmune disorders.

L20 ANSWER 13 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2002:370417 BIOSIS

DN PREV200200370417

TI A CD200Fc immunoadhesin prolongs rat islet xenograft survival in mice.

AU Gorczynski, Reginald M. [Reprint author]; Hu, Jiang [Reprint author]; Chen, Zhiqi [Reprint author]; Kai, Yu [Reprint author]; Lei, Ji [Reprint author]

CS Transplant Research Division, Toronto Hospital, 200 Elizabeth Street, CCRW 2-855, Toronto, ON, M5G2C4, Canada

SO FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1032. print.  
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.  
CODEN: FAJOEC. ISSN: 0892-6638.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 3 Jul 2002

Last Updated on STN: 3 Jul 2002

AB Background: A solubilized form of the cell surface CD200 molecule, CD200Fc, suppresses allograft rejection and development of collagen-induced arthritis in mice. We investigated whether the same molecule prolonged survival of rat islet xenografts. Methods: Streptozocin-treated mice, injected with anti-asialo-GM1 antibody, received rat islets (approx 400/mouse) under the kidney capsule or injected into the portal vein (pv), along with rapamycin treatment. Thereafter mice received injections of CD200Fc (10mg/mouse/injection) or control mouse IgG2. Blood glucose was monitored daily. Some mice received additional injections of anti-CD200/- \*\*\*CD200R\*\*\* mAbs. Results: Pv delivery of islets led to better sugar control than did transplantation under the kidney capsule. CD200Fc further prolonged survival in both groups, an effect abolished by anti-CD200 or F(ab')2 anti- \*\*\*CD200R\*\*\* mAbs, but not by whole anti- \*\*\*CD200R\*\*\*. Spleen cells taken from CD200Fc treated mice showed polarization to type-2 cytokine production (IL-4, IL-10) on restimulation with rat splenocytes in vitro, unlike cells from control mice (type-1 cytokines, IL-2, IFN $\gamma$ ). Conclusion: CD200/- \*\*\*CD200R\*\*\* interactions can regulate rat islet xenograft survival.

L20 ANSWER 14 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 7

AN 2002:576340 BIOSIS

DN PREV200200576340

TI Anti- \*\*\*CD200R\*\*\* ameliorates collagen-induced arthritis in mice.

AU Gorczynski, Reginald M. [Reprint author]; Chen, Zhiqi; Lee, Lydia; Yu, Kai; Hu, Jiang

CS Transplant Research Division, Toronto Hospital, 200 Elizabeth Street, CCRW 2-855, Toronto, ON, M5G 2C4, Canada

SO Clinical Immunology (Orlando), (September, 2002) Vol. 104, No. 3, pp. 256-264. print.  
ISSN: 1521-6616.

DT Article

LA English

ED Entered STN: 7 Nov 2002

Last Updated on STN: 7 Nov 2002

AB Immunization of DBA/1 with 100 mug bovine collagen type II emulsified in Freund's adjuvant, followed by booster injection in incomplete adjuvant at 18 days, leads to development of arthritis in more than 70% of mice by 28 days postinjection. We have previously shown that the novel immunosuppressant molecule CD200Fc (linking an extracellular domain of CD200 with a murine IgG2a Fc region) can suppress induction of disease when given to mice from the time of collagen injection. This occurs in concert with a decrease in the serum levels of anti-collagen IgG (approx 50% reduction), with relatively more IgG2b and IgG3, decreased serum levels of TNF $\alpha$  and IFN-gamma, and decreased production of those same cytokines after restimulation of lymphocytes in vitro with collagen. Since CD200 induces suppression following engagement of a receptor ( \*\*\*CD200R\*\*\* ), known to be expressed on, among other cells, macrophages, we investigated whether infusion of anti- \*\*\*CD200R\*\*\* and/or CD200Fc would ameliorate established disease in DBA mice, when injections were begun following collagen immunization. Our data indicate an arrest of disease following either treatment, with modification of a number of immune parameters (serum and lymphocyte cytokine production) consistent with a general role for CD200/- \*\*\*CD200R\*\*\* interactions in the regulation of induction and/or expression of autoimmune disorders. When a higher dose (250 mug/mouse) of anti- \*\*\*CD200R\*\*\* was infused into a group of overtly arthritic mice, a significant (approx 50%) decrease in arthritic joint score occurred over the 4-week treatment period.

L20 ANSWER 15 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2002:487666 BIOSIS

DN PREV200200487666

TI Microglial regulation through interaction with neuronal ligands triggering myeloid inhibitory and activating receptors.

AU Sedgwick, J. D. [Reprint author]; Hoek, R. H. [Reprint author]; Cherwinski, H. [Reprint author]; Phillips, J. [Reprint author]; Ruuls, S.

[Reprint author]; Murphy, C. [Reprint author]; Joyce-Shaikh, B. [Reprint author]  
 CS DNAX Research Inc., Palo Alto, CA, USA  
 SO Journal of Neurochemistry, (June, 2002) Vol. 81, No. Supplement 1, pp. 66.  
 print.  
 Meeting Info.: Thirty-Third Annual Meeting of the American Society for Neurochemistry, Palm Beach, Florida, USA. June 22-26, 2002.  
 CODEN: JONRA9. ISSN: 0022-3042.  
 DT Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 LA English  
 ED Entered STN: 18 Sep 2002  
 Last Updated on STN: 18 Sep 2002

L20 ANSWER 16 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
 INC. on STN  
 DUPLICATE 8  
 AN 2002:453404 BIOSIS  
 DN PREV200200453404  
 TI The same immunoregulatory molecules contribute to successful pregnancy and transplantation.  
 AU Gorczynski, Reginald M. [Reprint author]; Hadidi, Sima; Yu, Gary, Clark, David A.  
 CS Toronto Hospital, 101 College Street W., CCRW 2-855, Toronto, ON, M5G2C4, Canada  
 rgorczyński@uhnres.utoronto.ca  
 SO American Journal of Reproductive Immunology, (July, 2002) Vol. 48, No. 1, pp. 18-26. print.  
 ISSN: 1046-7408.  
 DT Article  
 LA English  
 ED Entered STN: 21 Aug 2002  
 Last Updated on STN: 21 Aug 2002

AB PROBLEM: At least two dendritic cell-associated molecules have been shown to contribute to the successful outcome of organ and tissue allografts in mice, namely CD200 and MD-1. CD200 is up-regulated in rodent transplantation models where successful inhibition of rejection is accomplished, and is believed to signal immunosuppression following engagement of a receptor, \*\*\*CD200R\*\*\*, on macrophages and/or gamma delta T-cell receptor (gamma delta TCR+ cells MD-1 is implicated in controlling expression of costimulatory molecules including CD80/CD86 which induce an immunorejection response, and thus inhibition of MD-1 expression also facilitates increased graft survival MD-1 also stabilizes expression of CD14, part of the receptor complex for LPS. As well as the inhibition of rejection which follows blockade of MD-1 expression and/or augmentation of CD200 expression, an altered polarization in cytokine production is seen, with increased expression of interleukin-4 (IL-4), IL-10 and transforming growth factor-beta (TGF-beta), and decreased IL-2, interferon-gamma (IFN-gamma) and tumor necrosis factor-alpha (TNF-alpha). Successful pregnancy in allografting mice also depends upon control of graft rejection mechanisms. Proinflammatory T-helper 1 (Th1) cytokines (TNF-alpha+IFN-gamma+ IL-1) have been shown to cause spontaneous abortion in mice by activating a novel prothrombinase, fibrinogen-like peptide (fibrinogen-like peptide) fgl2, which may promote fibrin deposition in the graft rejection process; expression of IL-10, TGF-beta, and progesterone-induced blocking factor (PIBF) in contrast leads to lowering of abortion rates. Interestingly, the spontaneous abortion rates in abortion-prone CBAXDBA/2 matings and in the low abortion rate CBAXBALB/c matings were lower than the frequency of implantation sites showing fibrin+fgl2 (mRNA)hi, implying regulation of the pro-abortion consequences of fgl2 expression. METHODS: We have investigated, by in situ hybridization, CD200, MD-1 and fgl2 expression in implantation sites in different strains of mice, and studied the effects of anti-MD-1, anti-CD200 and CD200Fc immunoadhesin on fetal and allograft survival. The role of indoleamine dioxygenase (IDO) was evaluated. RESULTS: CD200 mRNA expression occurred in the same sites as fgl2 mRNA. Anti-CD200 antibody raised the abortion rate to predicted levels, and infusion of a CD200 immunoadhesin reduced the abortion rate, as did an anti-MD-1 antibody. The latter also improved organ and tissue graft survival. Suppression by antigen-presenting macrophages triggered by CD200 is dependent upon intact IDO activity. CONCLUSION: Regulation of CD200 and MD-1 expression may control both pregnancy and allograft survival.

L20 ANSWER 17 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
 INC. on STN  
 AN 2003:143315 BIOSIS  
 DN PREV200300143315  
 TI Role of Myeloid Regulatory Molecule CD200 in Tolerance Induction Via the Nasal Mucosa.  
 AU Liversidge, J. M. [Reprint Author]; Dick, A.; Calder, C.; Sedgwick, J.; Taylor, N. [Reprint Author]  
 CS Ophthalmology, University of Aberdeen, Aberdeen, UK  
 SO ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 1544. cd-rom.  
 Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology, Fort Lauderdale, Florida, USA. May 05-10, 2002.  
 DT Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 LA English

ED Entered STN: 19 Mar 2003  
 Last Updated on STN: 19 Mar 2003

AB Purpose: A myeloid regulatory role for CD200 has been proposed since disruption of signalling via \*\*\*CD200R\*\*\* in animal models leads to an accumulation of DAP-12+ F4/80+ cells within normal lymphoid and non-lymphoid tissues predisposing the animal to autoimmune inflammation. The purpose of this study was to examine the phenotype and function of CD200-/- (KO) macrophages and dendritic cells compared to CD200+/+ (WT) in the context of tolerance induction to EAU via the nasal mucosa. Methods: Respiratory tract myeloid cells (RTMC), draining cervical lymph nodes (CLN), submandibular lymph nodes (SMLN) and spleens (SPL), from CD200 WT or KO C57Bl/6 mice were examined by FACS analysis and immunocytochemistry at time zero (control) or at intervals following instillation of IRBP peptide 1-20 (50ug) or PBS intranasally (minimum of 3 animals at each time point). Groups of 4 WT or KO animals were tolerised using 50mg peptide 1-20 or control PBS and then challenged 10 days later by immunisation with 500ug peptide 1-20 in FCS with pertussis toxin as additional adjuvant. Control mice were challenged with PBS in FCS. Eyes were taken at day 16 post immunisation and scored for retinal damage. Results: FACS analysis of RTMC indicated that cells were of an immature APC phenotype and expressed lower levels of MHC class II than WT. Significant reductions in MHC Class II+ expression by both dendritic cells and macrophages in lymphoid tissue from KO mice were also found. Image analysis of immunostained sections of lymphoid tissue sampled from animals at 0-48h post intranasal challenge with peptide 1-20 confirmed this and that low MHC class II expression by KO cells persisted for up to 48h. STAT-4 expression by both WT and KO lymphoid cells was generally weak, although a few strongly positive cells were observed at 24-48 hours. In contrast, STAT 6 was strongly expressed particularly by WT cells and was increased over time with strongest expression in T cell areas of CLN at 4h-48h. Conclusion: Although the DAP-12 activated phenotype of myeloid cells from CD200-/- mice pre-disposes these animals to autoimmunity the activation phenotype does not appear to extend to MHC class II expression or dominant expression of Th1 signalling STAT4 protein in our model. However, dominant expression of STAT6 Th2 signalling protein may contribute to the low levels of EAU pathology in the C57Bl/6 mouse and the reduced MHC class II expression that we observed.

L20 ANSWER 18 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS  
 INC. on STN  
 DUPLICATE 9  
 AN 2001:429194 BIOSIS  
 DN PREV200100429194  
 TI Transplant tolerance modifying antibody to CD200 receptor, but not CD200, alters cytokine production profile from stimulated macrophages.  
 AU Gorczynski, Reginald M. [Reprint author]  
 CS Toronto Hospital, 200 Elizabeth Street, CCRW 2-855, Toronto, ON, M5G2C4, Canada  
 SO European Journal of Immunology, (August, 2001) Vol. 31, No. 8, pp. 2331-2337. print.  
 CODEN: EJIMAF. ISSN: 0014-2980.  
 DT Article  
 LA English  
 ED Entered STN: 12 Sep 2001  
 Last Updated on STN: 22 Feb 2002

AB Increased C57BL/6 allograft survival following donor-specific dendritic cell (DC) portal vein (pv) pre-transplant immunization of C3H mice is associated with increased expression of the molecule CD200 on DC, delivery of suppressive signals by \*\*\*CD200R\*\*\* + macrophages, and polarization in cytokine production towards type-2 cytokines. Infusion of anti-mouse CD200 monoclonal antibody abolishes these effects. We have used whole Ig, and F(ab')2 fragments, of anti-CD200 and anti-\*\*\*CD200R\*\*\* mAb to explore the relative signaling role of CD200+ versus \*\*\*CD200R\*\*\* + cells in suppression of type-1 cytokine production in mixed leukocyte cultures (MLC), and enhanced graft survival in vivo. Simple neutralization of CD200 (even by F(ab')2 antibody) reversed CD200-mediated suppression. However, only whole anti-\*\*\*CD200R\*\*\* antibody was effective in stimulating suppression from \*\*\*CD200R\*\*\* + cells. Suppression of cytokine induction following cross-linking of \*\*\*CD200R\*\*\* + cells in vitro was attenuated by anti-IL-6 mAb. Our data are consistent with the hypothesis that \*\*\*CD200R\*\*\* itself delivers the crucial intracellular signal leading to immunosuppression, a feature likely of importance in autoimmunity and transplantation.

L20 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2001:687850 CAPLUS  
 DN 136:245923  
 TI Does successful allopregnancy mimic transplantation tolerance?  
 AU Gorczynski, Reginald M.; Yu, Gary, Clark, David A.  
 CS RM CCRW-2-855, Toronto Hospital, Toronto, ON, M5G2C4, Can.  
 SO Graft (Thousand Oaks, CA, United States) (2001), 4(5), 338-345  
 CODEN: GTOCA5; ISSN: 1522-1628  
 PB Sage Science Press  
 DT Journal; General Review  
 LA English  
 AB A review. The dendritic-cell assoc. mol. CD200 is up-regulated in rodent transplantation models where successful inhibition of rejection is accomplished. The mechanism by which CD200 achieves this effect involves signaling a receptor, \*\*\*CD200R\*\*\*, on macrophages and/or gamma..delta.TCR+ cells, both of which have been implicated in adoptive transfer of tolerance. In addn. to inhibition of rejection, increased

expression of CD200 is assocd. with altered polarization in cytokine prodn., with increased expression of IL-4, IL-10 and TGF beta., and decreased IL-2, IFN gamma. and TNF. alpha.. Inhibition of rejection can thus be adoptively transferred by IL-10/TGF. beta. and a CD200 immunoadhesin and in turn can be inhibited by neutralizing these cytokines or by functional blockade of CD200 expression. Successful pregnancy in allograft mice can also be viewed as dependent upon control of graft rejection. Proinflammatory Th1 cytokines (TNF. alpha. + IFN. gamma. + IL-1) can cause spontaneous abortion in mice by a mechanism which involves a novel prothrombinase, fgl2, which promotes fibrin deposition. However, we found that spontaneous abortion rates in abortion-prone CBA. times. DBA/2 matings and in low abortion rate CBA. times. BALB/c matings were lower than the frequency of implantation sites showing fibrinhi + fgl2 mRNAhi. CD200 expression was present in the same sites as fgl2 mRNA, and neutralization of this CD200 expression by anti-CD200 antibody raised the abortion rate to predicted levels. Conversely, a CD200 immunoadhesin dramatically reduced the abortion rate. We hypothesize that in addn. to its role in organ and tissue allograft rejection, CD200 expression is involved in the prevention of spontaneous abortion triggered by cytokine up-regulation of fgl2 at the feto-maternal interface.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 20 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 10

AN 2001:578114 BIOSIS

DN PREV200100578114

TI Evidence of a role for CD200 in regulation of immune rejection of leukaemic tumour cells in C57BL/6 mice.

AU Gorczynski, R. M. [Reprint author]; Chen, Z.; Hu, J.; Kai, Y.; Lei, J.

CS The Toronto Hospital, 200 Elizabeth Street, CCRW 2-855, Toronto, Ontario, M5G2C4, Canada

rgorczynski@transplantunit.org

SO Clinical and Experimental Immunology, (November, 2001) Vol. 126, No. 2, pp. 220-229. print.

CODEN: CEXIAL ISSN: 0009-9104.

DT Article

LA English

ED Entered STN: 12 Dec 2001

Last Updated on STN: 25 Feb 2002

AB Increased expression of the molecule CD200 in mice receiving renal allografts is associated with immunosuppression leading to increased graft survival, and altered cytokine production in lymphocytes harvested from the transplanted animals. Preferential production of IL-4, IL-10 and TGFbeta occurs on donor-specific restimulation in vitro, with decreased production of IL-2, IFNgamma and TNFalpha. These effects are enhanced by simultaneous infusion of CD200 immunoadhesin (CD200Fc) and donor CD200 receptor ( \*\*\*CD200r\*\*\* ) bearing macrophages to transplanted mice. C57BL/6 mice do not normally resist growth of EL4 or C1498 leukaemia tumour cells. Following transplantation of cyclophosphamide-treated C57BL/6 with T-depleted C3H bone marrow cells, or for the EL4 tumour, immunization of C57BL/6 mice with tumour cells transfected with a vector encoding the co-stimulatory molecule CD80 (EL4-CD80), mice resist growth of tumour challenge. Immunization of C57BL/6 mice with EL4 cells overexpressing CD86 (EL4-CD86) is ineffective. Protection from tumour growth in either model is suppressed by infusion of CD200Fc, an effect enhanced by co-infusion of \*\*\*CD200r\*\*\* + macrophages. CD200Fc acts on both CD4+ and CD8+ cells to produce this suppression. These data are consistent with the hypothesis that immunosuppression following CD200- \*\*\*CD200r\*\*\* interaction can regulate a functionally important tumour growth inhibition response in mice.

L20 ANSWER 21 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2001:557960 BIOSIS

DN PREV200100557960

TI Role of CD200: \*\*\*CD200r\*\*\* interactions in regulating islet xenograft rejection.

AU Gorczynski, R. [Reprint author]; Hu, J. [Reprint author]; Kai, Y. [Reprint author]; Wong, A. [Reprint author]; Lei, J. [Reprint author]

CS Toronto Hospital, Toronto, Canada

SO Xenotransplantation, (August, 2001) Vol. 8, No. Supplement 1, pp. 79. print.

Meeting Info.: VI Congress of the International Xenotransplantation Association. Chicago, Illinois, USA. September 29-October 03, 2001.

ISSN: 0908-665X.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

Conference; (Meeting Poster)

LA English

ED Entered STN: 5 Dec 2001

Last Updated on STN: 25 Feb 2002

L20 ANSWER 22 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2001:558262 BIOSIS

DN PREV200100558262

TI Regulation of MD-1 expression controls skin xenograft rejection.

AU Hadidi, S.; Gorczynski, R.

SO Xenotransplantation, (August, 2001) Vol. 8, No. Supplement 1, pp. 78. print.

Meeting Info.: VI Congress of the International Xenotransplantation Association. Chicago, Illinois, USA. September 29-October 03, 2001. ISSN: 0908-665X.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

Conference; (Meeting Poster)

LA English

ED Entered STN: 5 Dec 2001

Last Updated on STN: 25 Feb 2002

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TOTAL	

CA SUBSCRIBER PRICE	ENTRY	SESSION
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